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BRITISH SURGICAL PRACTICE

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BACKACHE

By HENRY COHEN, M.D., F.R.C.P., F.F.R.
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1. DEFINITION

46.] Backache is a symptom, not a disease, even when labelled "lumbago". It is among the initial complaints of one in every ten patients and presents major and formidable diagnostic problems which lie properly within the field of general medicine, though its treatment may need the services of one or more specialists. Its intensity varies from a trifling and fleeting discomfort to a prolonged and crippling disability. Its history teaches many lessons to the discerning; it is a graveyard in which are buried once-fashionable methods of treatment which were founded on a speculative pathology; the ghosts of these are restless, and one must beware of their reappearance even when clothed in different garb.

2. THE CAUSES OF BACKACHE

The causes of backache are conveniently classified and discussed as (1) spinal, (2) visceral, (3) nervous and (4) psychological.

(1) Spinal causes

The term "spinal" is used to cover all the skeletal structures of the back—bones, joints, ligaments, intervertebral discs, muscles, fasciae and fatty supporting tissues. These are all subject to the diseases and injuries which may affect similar structures elsewhere in the body, and they react to them in a similar manner; pain in the back is a common feature of all spinal lesions.

Disease of vertebrae

When the vertebrae are the seat of gross disease the presenting signs are (i) pain in the back, (ii) local tenderness on percussion of the spines of the affected vertebrae, (iii) rigidity of the affected portion of the spine, and often (iv) deformity and (v) radiological changes are found. In fractures and Kümmell's disease, dislocations and subluxations, including spondylolisthesis, tuberculous caries and malignant metastases, especially from breast and prostate, the diagnosis is usually obvious from the history and examination; but rarer conditions—senile and menopausal osteoporosis, osteitis deformans, osteomalacia, hyperparathyroidism, osteomyelitis, syphilitic osteitis, epiphyseal osteochondrosis (Scheuermann's disease) and primary neoplasms especially

Rarer conditions

The sacro-iliac joints, which are modified diarthroses, are subject to similar pathological lesions. *Sacro-iliac joints*

The intercentral joints are amphiarthrodial. Their importance lies in the discovery in recent years of the part played by lesions of the intervertebral discs in the production of low back pain and sciatica. These include retropulsion of the disc, herniation of the nucleus pulposus, both postero-lateral and anterior, calcification of the disc and Schmorl's nodes; they often follow strain and injury and give rise to episodes of low back pain, usually associated with pain in the back of the thigh, brought on by such work as digging in the garden or lifting heavy weights. In the more severe cases the signs and symptoms are due to spasm of the erector spinae muscles, and consist of (i) unilateral sciatic pain and paraesthesiae aggravated by coughing, sneezing or straining at stool, (ii) flattening of the normal lordotic curve of the lumbar spine with painful and limited flexion and extension of the spine, (iii) painful and limited flexion of the hip with the knee extended (Lasègue's sign) and (iv) a total scoliosis ("sciatic scoliosis") aggravated by flexion of the spine, usually away from the side of pain. Spasm of the erector spinae may result not only from disc lesions, but also from strains of the muscles, fasciae and ligaments of the lower back and from intervertebral arthritis. It is when "sciatic scoliosis" is accompanied by evidence of pressure on spinal nerves (especially the fourth or fifth lumbar), namely, sensory loss, muscle wasting and absent tendon reflexes—especially the ankle jerk, because of the common site of disc lesions—that the diagnosis of a disc lesion is strengthened. Here, too, it must be remembered that these are the signs of compression of the nerve root by any "tumour" and that the herniated nucleus pulposus or retropulsed disc is but one of the "tumours", albeit by far the commonest, which give rise to these pressure signs. Other "tumours" of the spinal cord, nerve roots or meninges, especially neuromas and meningiomas, thickening of the meninges in pachymeningitis, osteophytes in osteoarthritis, and hypertrophy of the ligamenta flava may give a similar clinical picture. *Intervertebral discs* *Signs and symptoms*

Rarely a ruptured disc occurs at other levels, for example, in the cervical region giving retronuchal pain radiating to one or both arms, and in the lower dorsal region causing interscapular pain and constriction of the chest, mimicking angina pectoris; a large rupture may compress the spinal cord or cauda equina. It is well to recall that manipulation of the spine for backache has occasionally resulted in a compression paraplegia due to further displacement of a pathological disc.

Lesions of the thick mass of spinal muscles and the strong inelastic fibrous ligaments attached to the vertebral bodies and their processes are of great importance in the pathogenesis of backache, though both in diagnosis and treatment much confusion arises because of our restricted knowledge of their exact pathology. Backache is a prominent feature of the onset of some acute infections—for example, influenza and smallpox—and accompanies most. In these and other forms of acute myositis—infective, parasitic and traumatic—the diagnosis is made from the recent history and evidence of infection or injury, and the localized muscle tenderness and swelling. *Spinal muscles and ligaments*

It is in the diagnosis and treatment of strains, both acute and chronic, that there is a tendency to surrender judgement to the fascination of a name. Muscles, fasciae, ligaments or joint capsules may alone or in combination be

osteogenic sarcoma, haemangioma, and Ewing's tumour, must not go unheeded. Moreover, extra-vertebral lesions which erode or invade the vertebral column such as aortic aneurysm, retroperitoneal tumours, cancer of paravertebral structures, e.g. of the pancreas, oesophagus, rectum and other pelvic organs, will give similar clinical signs.

Less evident injuries

It is important not to overlook the less evident injuries, such as fractures of the vertebral spines, transverse processes and laminae, and stellate fractures of the vertebral body, as causes of back pain, and to remember that even in the absence of x-ray evidence, every persistent pain in the back which appears after an operation for cancer, no matter how long the interval between the operation and the appearance of pain, must be regarded as due to metastases until the contrary is proved.

Coincidental deformities

Here also a warning must be sounded against regarding vertebral abnormalities revealed by skiagrams as the necessary cause of the patient's backache. Congenital deformities are found in nearly a third of all spinal radiographs. They include wedge-shaped (hemivertebrae), spina bifida occulta, sacralization of the fifth lumbar vertebra, lumbarization of the first sacral vertebra, abnormally placed and directed articular facets especially lumbo-sacral, spondylolysis, posterior displacement of the fifth lumbar vertebra, and abnormal vascular grooves. Impingement of the spinous processes and constriction of the intervertebral foramina may be congenital, but in degeneration of the intervertebral disc both changes may occur associated with narrowing of the intervertebral space. Lipping of the vertebral margins is so common as to be rarely absent after middle age. All these lesions, both congenital and acquired, may be coincidental. Their role in the pathogenesis of backache is that they predispose to muscle, joint and ligamentous strains, and these strains must be demonstrated before the bony abnormality is regarded as causal or contributory.

Vertebral articulations

The vertebrae present two sets of intrinsic articulations, (i) intercentral, between the bodies, and (ii) interneural, the paired articulations between the neural arches. The articulations of the spine with the pelvis and the ribs—the sacro-iliac joints and the costo-vertebral joints (both costo-central and costo-transverse)—are also important seats of disease causing backache.

Arthritis

The interneural and costo-vertebral joints like other diarthroses with capsules, synovial membranes and articular cartilages may be attacked by any of the arthritic diseases, namely (i) infective (those due to infection with the typhoid and dysentery group, gonococcus, streptococcus, pneumococcus, tuberculosis, syphilis and brucellosis are the commonest); (ii) rheumatoid (spondylitis ankylopoietica); (iii) degenerative (spondylitis osteoarthritica and spondylitis muscularis); (iv) metabolic (gout and ochronosis); (v) allergic; (vi) traumatic; (vii) in haemophilia and other haemorrhagic diseases; and (viii) neuropathic (Charcot's joint). Although Charcot's joint of the spine, especially in the lumbar region, is not uncommon it is often overlooked because pain is usually absent at the site of the lesion, though the strain it imposes may cause pain higher up the back.

Arthritis is associated with (i) pain, which is worse on rising after a night's rest, but in the early stages improves with the day's activities, (ii) local tenderness, (iii) limitation of movement of the affected part of the spine in all directions, and often (iv) local muscle spasm.

Distinction between muscular and ligamentous strains

To distinguish between muscular and ligamentous strains is usually simple. The ligamentous adhesion causes pain when it is stretched; the muscular, both when it is stretched and when the affected muscle contracts. For example, if stooping is painful and limited but rising eases the discomfort, the strain is ligamentous. If stooping is painful and the discomfort is aggravated by straightening the spine—when the muscles of the back are contracting to raise the weight of the body—the strain is muscular. Similarly sacro-iliac strain can be differentiated from gluteal strain by the following simple test. The patient lies prone and relaxed, and the thigh of the painful side is passively extended. This causes severe pain in sacro-iliac strain because the ligaments of the joint are stretched, but in muscular strain this manoeuvre is practically painless. If active extension of the thigh in this position is painful, then the strain is muscular, because the patient can rarely achieve by muscular contraction sufficient extension of the thigh at the hip to stretch the sacro-iliac ligaments and produce pain. If both muscular and ligamentous strains are associated, the signs are mainly those of the muscular strain.

Treatment of strains

The importance of appreciating this conception of strain is emphasized in the principles of its treatment. During the acute stage rest in bed and sedatives are imperative to aid the absorption of the blood and lymph exudate. While the adhesions are still vascular gentle movements and physiotherapy will help to stretch them. Manipulation must clearly be avoided at this early stage, for it causes fresh damage and retards progress. When, however, the fibrous tissue is established, then manipulation is necessary, and it is here that the differentiation of ligamentous and muscular strains is so important. Manipulation may act by snapping an adhesion or by reproducing the condition of acute strain which if competently treated leads to cure. If manipulation is carried out under a general anaesthetic which gives complete muscular relaxation, ligamentous adhesions can be broken down easily and successfully. But this very muscular relaxation prevents such a manipulation from breaking down muscular adhesions; all it achieves is the taking up of the resultant slack. Hence muscular strains must be manipulated with the aid of a local anaesthetic; the painful area is infiltrated with a solution of procaine hydrochloride and the muscle is stretched by the patient's carrying out movements which were previously painful. For example, for chronic strain of the right sacrospinalis he carries out full forward and left lateral flexion of the trunk aided by his own weight; this is followed by full contraction of the muscle by extension and right lateral flexion against resistance. A feeling of bruising which may last a few days follows such manipulation; the increased range of movement it secures must be maintained by exercises, heat and massage for a fortnight or more. Occasionally, adhesions are so dense that they must be cut or excised.

Backache and stiffness may appear abruptly without a recognized history of trauma, or of infection, and with no other physical sign than occasional nodules of varying size, which may be tender but are often painless, in the affected area. The condition is then often diagnosed as "fibrositis" or "lumbago" and ascribed to a rheumatic cause—infection, cold, damp, worry and so on. It is well to remember that, whilst infections of muscular aponeuroses may occur, most cases of "fibrositis" cannot yet be defined in terms of any exact pathology. The diagnosis of "fibrositis" remains unconvincing. It is justified

"Fibrositis"

Iuscular and igamentous trains

the seat of strain. Gross bony injury, for example, fracture of a vertebral spine, may accompany such strains, and clearly where this occurs treatment must be directed towards it as well as to the strain. Where the strain involves joint structures the signs are those of arthritis.

Acute strain

Acute strain results from injury, either (i) direct (a blow), or (ii) indirect (a sudden twist of the back or lifting a heavy weight). The intensity of the pain may bear no apparent relationship to the severity of the injury which causes it. Ninety per cent of strains occur in the lower back (lumbo-sacral and sacro-iliac regions), for it is here that man's erect posture imposes the greatest mechanical stress; the lumbo-sacral joint is the major fulcrum of the body. Resulting from the injury a tear of muscle or ligament occurs; except from direct blows this is rarely found in the main body of the muscle or ligament; the tear occurs at the attachment of the ligament to bone or to joint capsule, or where the muscle is attached to its tendon or where the tendon is inserted into bone—that is to say, where a more elastic tissue meets a less elastic or non-elastic tissue. The muscle aponeuroses have a fibrous tissue structure which through lateral shear permits a slight but definite range of movement, but their reaction to injury is essentially that of ligaments. The tear leads to haemorrhage and oedema with local tenderness and swelling; the swelling is due not only to the accompanying exudate but also to protective muscle spasm. The pain which results is not confined to the injured part, but may be referred to the whole of the corresponding segmental nerve supply, hence the common reference of pain to the groin and lower limbs in low backache. All pain and accompanying muscular rigidity can be relieved by injecting a solution of procaine hydrochloride locally into the damaged area.

Rapid resolution of the exudate is initiated by an outpouring of fibroblasts into the damaged tissues; gradually fibrosis occurs, and in the absence of treatment this may lead to scars or adhesions in muscles, joints or ligaments which give the signs of a chronic strain. Chronic strain, however, may result not only from inadequately treated acute strains, but also from repeated and prolonged unusual stress on muscles or ligaments occasioned by faulty postures or by vertebral abnormalities; as has been earlier emphasized, these abnormalities act by setting up abnormal muscle and ligamentous strains. The tendency to strain is, moreover, increased when the muscles are weakened by prolonged illness, obesity, sedentary occupation, or lack of exercise. It must also be remembered that abnormal back stresses may be secondary to deformities and disease in the lower limbs. Ober (1936) has emphasized the role of a contracted fascia lata in low back pain.

Chronic strain

Chronic strain is the commonest cause of backache. The pain, which often disappears after a night's rest and reappears with activity as the day advances, is caused by stretching fibrous adhesions. These adhesions limit the range of movement only in the direction of their stretching. Thus strain can be differentiated from arthritis; in strain the range of certain movements only is restricted, whilst in arthritis movements are limited in all directions. Moreover, if movement of the spine is kept within the range imposed by the adhesions, the patient may remain quite comfortable, but any sudden movement beyond that range may cause a fresh tear and reproduce the cycle of acute strain except where the sudden movement snaps an adhesion; then cure of the patient's backache may result.

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The importance of appreciating this conception of strain is emphasized in the principles of its treatment. During the acute stage rest in bed and sedatives are imperative to aid the absorption of the blood and lymph exudate. While the adhesions are still vascular gentle movements and physiotherapy will help to stretch them. Manipulation must clearly be avoided at this early stage, for it causes fresh damage and retards progress. When, however, the fibrous tissue is established, then manipulation is necessary, and it is here that the differentiation of ligamentous and muscular strains is so important. Manipulation may act by snapping an adhesion or by reproducing the condition of acute strain which if competently treated leads to cure. If manipulation is carried out under a general anaesthetic which gives complete muscular relaxation, ligamentous adhesions can be broken down easily and successfully. But this very muscular relaxation prevents such a manipulation from breaking down muscular adhesions; all it achieves is the taking up of the resultant slack. Hence muscular strains must be manipulated with the aid of a local anaesthetic; the painful area is infiltrated with a solution of procaine hydrochloride and the muscle is stretched by the patient's carrying out movements which were previously painful. For example, for chronic strain of the right sacrospinalis he carries out full forward and left lateral flexion of the trunk aided by his own weight; this is followed by full contraction of the muscle by extension and right lateral flexion against resistance. A feeling of bruising which may last a few days follows such manipulation; the increased range of movement it secures must be maintained by exercises, heat and massage for a fortnight or more. Occasionally, adhesions are so dense that they must be cut or excised.

"Fibrositis"

Backache and stiffness may appear abruptly without a recognized history of trauma, or of infection, and with no other physical sign than occasional nodules of varying size, which may be tender but are often painless, in the affected area. The condition is then often diagnosed as "fibrositis" or "lumbago" and ascribed to a rheumatic cause—infection, cold, damp, worry and so on. It is well to remember that, whilst infections of muscular aponeuroses may occur, most cases of "fibrositis" cannot yet be defined in terms of any exact pathology. The diagnosis of "fibrositis" remains unconvincing. It is justified

only as a provisional label when every effort has failed to unmask an adequate cause of backache. Disappearance of pain in alleged fibrositis may efface a problem; persistence of pain is a signal for a detailed review of its aetiology.

Panniculitis

Herniae of fat

Two rare conditions associated with painful nodules are occasionally seen. First, panniculitis, which is an inflammation of the subcutaneous fatty tissue. It may occur associated with other rheumatic manifestations or in the form of Weber-Christian disease, a febrile relapsing nodular non-suppurative panniculitis. Secondly, Copeman and Ackerman (1944) have described herniae of the fat surrounding the spinal muscles through gaps in their aponeuroses; these are "trigger points" which if pressed or stretched will reproduce the pain of which the patient complains; removal of these fatty herniae cures the pain.

Coccygodynia

Special attention should be paid to pain in the sacro-coccygeal region (coccygodynia). This is practically confined to females and usually attributed to injury, such as a fall or a kick. The pain is aggravated by sitting on a hard surface (the victim often carries a cushion or an air ring with her) or on rising after sitting. It may radiate to buttocks and legs and occasionally is associated with painful defaecation. Rectal examination often reveals tenderness on pressure over the coccyx; spasm of the levator ani, coccygeus, and pyriformis muscles accompanying the pain has been described. A skiagram may reveal old injury or deformity of the coccyx. The immunity of the male is attributed to his narrow sacro-iliac notches, and his relatively longer ischial tuberosities which thus tend to shield the coccyx. The main factors, however, in the genesis of coccygodynia in the majority of patients are undoubtedly psychogenic. In most cases treatment, even removal of the coccyx, is of transient benefit, and not infrequently it intensifies the patient's complaints.

Psychogenic factors

Segmental reference of "spinal" pain

In relation to pain arising from spinal structures it should be recalled that their sensory nerve supply is derived mainly from the posterior primary divisions of the spinal nerves. Irritation of any branch or twig may cause pain, hyperaesthesia, and muscular rigidity referred to the entire segmental distribution of the spinal nerve from which it arises; hence the common occurrence of pain in the back of the thigh with sacro-spinalis strain. All pain—both local and referred—is abolished by anaesthetization of the site of the lesion responsible for the pain. This test will help to distinguish referred sciatic pain from that due to direct pressure on one of the roots of the sciatic nerve from, for example, a ruptured intervertebral disc or spinal tumour, but the test must not be regarded as pathognomonic.

(2) Visceral causes

"True" visceral pain

Disease of the thoracic, abdominal and pelvic viscera commonly gives rise to pain in the back, and occasionally this pain is the patient's main complaint. Visceral pain arises from two sources: (a) from the viscus itself ("true" visceral pain), and (b) from involvement of contiguous structures by spread of disease from the viscus. That from the viscus itself is due to abnormal tension of its muscular wall, for example, colic arises from spasm in obstruction or from distension in ileus; this may result in ischaemia of the muscle as in angina of effort, cardiac infarction, or the anginal pain of severe anaemias. This true visceral pain is felt in the distribution of the segmental nerve supply of the viscus; with non-paired organs it is felt in the midline of the body, usually anteriorly but not infrequently in the back, which may be its only site; the pain

is deep, ill-localized and unrelated to posture or movements of the spine; it is excited by any factor which increases muscle tension or ischaemia. Hence pain in the interscapular region excited in a few seconds or minutes by exertion or cold and relieved by rest and warmth has a cardiac or aortic origin; pain in the same site brought on by swallowing may well arise in oesophageal disease—cardiospasm, stricture or para-oesophageal hernia. Similarly, pain in the sacral region relieved by the onset of the menstrual flow or the passage of a clot *per vaginam* points to a uterine lesion. Unilateral involvement of paired viscera, for example kidney or lung, gives homolateral back pain, as in pyelectasis from stone or pelvi-ureteric stricture when pain is felt in the loin of the same side; in bilateral renal lesions, such as acute nephritis or chronic pyelonephritis, diffuse lumbar ache or pain does occasionally occur, but contrary to popular belief—and the apprehensions born of lurid patent-medicine advertisements—lumbar pain very rarely implies underlying kidney disease.

Contiguous visceral disease

The second source of visceral pain is of greater importance. The serous membranes and spinal structures are all sensitive, and when invaded or stretched by contiguous visceral disease they give rise to pain which is fairly accurately localized and is often accompanied by muscular rigidity. Reference has already been made to involvement of the spine by direct spread of disease, in retroperitoneal tumours and in vertebral erosion from aneurysms; these give the signs of vertebral disease. When the peritoneum of the posterior abdominal wall is involved by a visceral lesion, for example an adherent juxta-pyloric ulcer, an inflamed trans-abdominal appendix or parametritis, pain in the back is common and often severe; its surface localization corresponds to the area overlying the involved peritoneum.

(3) Nervous causes

Backache is a rare complaint in organic disease of the nervous system, and when present it is usually overshadowed by the accompanying disabilities of paralysis, sensory loss and loss of sphincter control, or by the radicular pains which are referred segmentally to trunk or limbs. Intense backache, however, may occur:

(a) With meningeal irritation, when it is accompanied by marked extensor rigidity of the spine, as in spinal meningitis, the onset of poliomyelitis, spinal subarachnoid haemorrhage, the extension of a medulloblastoma or carcinomatosis in the spinal meninges, or a large tumour filling the spinal canal (especially seen in the lumbo-sacral region);

(b) Where posterior nerve roots or ganglia are irritated, as in tabes dorsalis, herpes zoster, pachymeningitis, gummas and, rarely, other granulomas, and spinal tumours;

(c) When the nervous disease results in either (i) muscular paralysis in which the ensuing deformity or abnormal posture gives rise to chronic strain, for example in myelopathies, myopathies and syringomyelia, or (ii) in muscular rigidity or spasm, as in Parkinsonism. In an analysis of 500 consecutive cases of different types of organic disease of the nervous system only 7 gave backache as their dominant and presenting symptom; but over 20 per cent on direct questioning gave an affirmative answer when asked if they had backache.

(4) Psychological causes

Associated psychological factors

Even in the presence of organic disease the contribution of associated psychological factors must not be overlooked. The threshold for pain varies from patient to patient. Identical lesions cause in one patient "excruciating pain", whilst another complains of a trifling "ache". In the worrier, backache might conjure up grave or fatal possibilities such as Bright's disease, and thus results a psychoneurosis which intensifies or prolongs the complaint; for the phlegmatic, a diagnosis of "lumbago" satisfies, and dispels anxiety.

Primary psychological disorders might in the absence of any organic disease give rise to backache; or an organic cause might long since have passed or might be so slight that no complaints would be made were it not for the co-existence of the psychological disorder. Conditions in the Services in World War II have given unusual opportunities for the study of this group.

The frank malingerer is most uncommon and easily recognized. The two main psychological types encountered are those suffering (i) from hysteria and (ii) from anxiety neuroses. The term hysteria must be used in its restricted sense of a psychogenic reaction which serves a personal purpose; the illness thus induced allows the patient to escape from a difficulty or to fulfil a desire, real or fanciful. The hysterical patient is in varying degree unaware of his motivation; the malingerer is deliberately and consciously feigning illness; but there are all stages of transition between hysteria and malingering.

Hysterical backache

Hysterical backache is of three types: (a) when there is a complaint of backache and an hysterical imitation of the signs thought to be associated with it (simple conversion hysteria); this is very rare and easily recognized; (b) when evidence of organic disease is found, usually due to an old injury which has been symptomless for years, but the backache appeared when the patient was exposed to the stress and hazards of military service; (c) when backache persists after the effects of an injury or illness should long have passed; this is frequently seen both in war injuries, for example, as a result of blast, and of crash landings, and also in civilian injuries, especially when the question of compensation is involved. The diagnosis of hysteria must not depend solely upon the exclusion of physical or other mental diseases which would of themselves be adequate to account for the backache. Positive evidence of psychogenic factors which are sufficient to explain a persistent backache must be demonstrated, and here the personality of the patient, his past history and his present behaviour are most significant.

Anxiety neurosis

By far the largest number of psychogenic backaches fall into the anxiety neurosis group. The backache in anxiety states is due to muscular tension, which is the somatic manifestation of the increased nervous tension. Here, fear is the cause; for example, fear of the return to active combat or fear of the backache being the sign of grave illness. This anxiety syndrome is accompanied by the characteristic visceral disturbances of "preparing for action", —palpitation, mammary pain, breathlessness, sweating, tremor, exaggerated tendon reflexes, exhaustion, insomnia, fearful dreams and restlessness. Unlike the hysteric who rejoices in his disability and accepts his "agonizing torments" with unnatural resignation, the patient with an anxiety neurosis is tense and nervous, and the more restless he is the worse is his backache. The site of his pain is usually lumbo-sacral, but it may be referred to any part of the spine and is often diffuse; it is usually intermittent though worse at night, in

the early morning, after exercise, or after long sitting or standing. Associated spasm in the sacro-spinalis and erector spinae muscles can often be palpated, and even fibrillary twitchings and fasciculation may be seen. This spasm may limit flexion of the spine and give a Lasègue's sign.

These psychogenic factors in backache need careful appraisal in differential diagnosis, especially in relation to accompanying organic disease where their contribution to the cause or persistence of pain is so significant in treatment and prognosis.

3. EXAMINATION OF THE PATIENT WITH BACKACHE

The discussion of the causes of backache demonstrates clearly that the first stage in diagnosis lies with the general practitioner or general physician. When the patient is assigned to his appropriate group more specialized help in diagnosis and treatment should, when necessary, be sought. The dangers of too early reference to the specialist are twofold. First, he is apt to overemphasize the part played by his own speciality in the aetiology of the patient's complaint; and secondly, he tends to attribute the temporary improvement which may follow his specialized treatment to the particular manoeuvre he has used rather than, as is so often the case, to a non-specific beneficial response which in the neurotic may result from any novel form of treatment. Just as the patient with a visceral neurosis may experience a period of apparent benefit after removal of the appendix, a nephropexy or a pelvic operation, so the patient with backache resulting from psychogenic factors may be temporarily relieved by manipulation or operation, but the recurrence of symptoms or a new group of complaints in a few months' time reveals the persistence of the original cause. A long-term follow-up of many methods of treatment for backache would disappoint their most sanguine and enthusiastic advocates.

Children

In children, muscles and ligaments are more resilient than in adult life, and rarely do they show either acute or chronic strain. Back pain in the child usually results from intrinsic disease of the spine or of abdominal or pelvic viscera. The exanthemata and other acute infections are in childhood often heralded by backache.

General physical examination

All patients with backache must have a general physical examination. The detailed findings in the manifold lesions which may be responsible for backache are given in their respective sections. Here a résumé of the essential points is made.

History

A well-documented and detailed history is, as in most disease, essential for accurate diagnosis, and should provide answers to the following questions: What is the patient's occupation? What stresses does it entail? What is the patient's posture at work? Has he recently changed his job?

Past history

Family history

In the past history, inquiry should be directed towards previous rheumatism, sore throat, gout, such infections as gonorrhoea, tuberculosis, syphilis, dysentery and typhoid fever, nervous and urinary disease, previous operations, especially prostatectomy and mastectomy, and similar attacks of backache in the past. The family history of rheumatic disorders should be explored. In the parous woman the history of her labours should be reviewed, especially if the backache followed childbirth.

Character of the pain

Of the pain itself the following points should be noted. When did it first occur and in what circumstances? Was the onset sudden or gradual? Was it related to injury or unusual effort such as lifting heavy objects, strenuous games, etc.? Did it follow an operation? When the pain appeared, was a "click" or "snap" heard or did the patient feel something "slip"? What is the site of the pain? Is it localized or diffuse and, if it spreads, where does it radiate? How intense is the pain and does the intensity fluctuate? What is its character? Is it sufficiently severe to keep the patient away from his work? Is the pain worsening, improving or stationary? Is the backache aggravated, eased or unaffected by any special posture, by rest or immobilization, by movement of the back or by prolonged activity or standing? Is it worse at any time of day or in certain weathers? Is it related to swallowing, flatulent eructations, meals or bowel movement; to coughing, straining, stooping, sneezing or lifting weights; to micturition; to menstruation or vaginal discharge; to worry, anxiety or stress? Have any medicines or treatment benefited or aggravated the pain? If the pain is chronic, has it been constant or recurring?

Interpretation of evidence

The physician must try to interpret the significance of the answers to these questions in terms of structural and functional disturbances and their cause. When visceral disease is suspected the appropriate interrogation concerning wasting, constipation or diarrhoea, piles, abnormalities of stool or urine, breathlessness, cough, expectoration, and so on must be made.

Examination of the back

The examination of the back must be conducted in a good light with the patient stripped. Faulty posture should be noted; this is evidenced by a forward position of the head, flattening of the chest, a protuberant and ptosic abdomen, exaggeration of the dorsal kyphosis and lumbar lordosis, downward tilt of the pelvis and hyper-extension of the knees.

Inspection of the spine and pelvis may reveal exaggerations or flattening of normal curves—scoliosis, lordosis, kyphosis and lateral tilting of the pelvis; the apparent trunk shortening with the exaggeration of lumbar concavity in spondylolisthesis should be noted. All movements of the spine and sacro-iliac joints must be tested and those which are limited or painful recorded; the lower limbs should be measured for asymmetry and muscular wasting; deformities of the feet, including pronation, should be looked for and other significant features, for example tumour masses, draining sinuses, and previous operation scars, must be observed. The shoes should be inspected.

Palpation of the back may disclose local or general tenderness and "trigger points", muscle spasm or wasting, and fluctuation in tumours. Percussion of the spines may cause marked local pain and show the site of a deep-seated lesion. Many special tests, e.g. Lasègue's, Goldthwait's, Ely's, Patrick's, Gaenslen's and other signs designed to differentiate between sciatic nerve, lumbo-sacral and hip lesions, and Ober's sign showing the presence of a tight ilio-tibial band, have been described. These eponymous signs, used by many as "penny in the slot" methods of diagnosis, give to them a false security. They are all but special examples of the general principles earlier enunciated, and should be interpreted in the light of these.

Cardiovascular and respiratory system examinations

In view of the possible thoracic and abdominal causes of backache, detailed attention must be paid to the examination of the cardiovascular and respiratory systems, and to the abdomen and pelvis. The cause of many a backache has been overlooked because a rectal or vaginal examination has been

neglected. A careful examination of the nervous system must include muscle power, wasting and fibrillation, tendon reflexes and sensation, especially in the lower limbs and perineum, in all cases of low backache.

Urine and blood examinations

The urine should be tested in all patients, and when indicated special pathological examinations should be made. These may include a blood count, and a differential white count; an erythrocyte sedimentation rate; blood chemistry, especially uric acid, calcium, phosphatase and sugar; Wassermann reaction; and agglutinations against enteric, dysentery and *brucella* organisms; the gonococcal fixation test has little specific value. When a neurological or disc lesion is suspected, cerebrospinal-fluid examination must be carried out; this should include manometry and the Queckenstedt test, the protein and cell content, the Wassermann reaction, and colloidal gold tests; these may help to throw light on the nature of the lesion.

Cerebrospinal-fluid examination

In arthritis, sources of infection, metabolic, allergic and other possible factors in the aetiology must be investigated.

X-ray examination

X-ray examination of the spine and pelvis is essential in persistent backache. A single antero-posterior view may fail to show such lesions as compression fractures, collapse of the body in metastatic malignancy, spondylolisthesis, and anomalies of the interneural articular facets. In all cases, therefore, a lateral view must also be taken, and in many instances both stereoscopic and oblique views will give helpful information especially about the sacro-iliac and lumbosacral joints. It is necessary to reiterate the warning that anomalies revealed by x-ray examination are but one of the pieces of clinical evidence leading to a diagnosis; the physician must not be misled into regarding such radiological changes as the inevitable cause of the patient's backache. Moreover, undue stress must not be laid upon negative x-ray findings in excluding the early stages of bone and joint disease, especially in spondylitis ankylopoietica, tuberculous caries, malignant metastases and osteomyelitis. Apart from direct skiagraphic demonstration of intrinsic bone and joint changes, including narrowing of the intervertebral spaces, radiography with Lipiodol (or Pantopaque) or air as contrast media to reveal filling defects may be used in the diagnosis of intraspinal lesions, including pathological discs. Lipiodol must, however, be used with great caution, and only if it is to be followed by an operation at which it can be removed. When a visceral or systemic cause of backache is suspected, skiagrams of the chest, alimentary and urinary tracts, electrocardiograms and other special methods of investigation may be needed in individual cases.

4. TREATMENT OF BACKACHE

Rational therapy

Too often analgesics, liniments, physiotherapy, or manipulation, are conditioned reflex responses to the complaint of "backache", but these are not panaceas. Recognition of the cause of backache is essential to its rational therapy. The detailed treatment of the various lesions giving rise to backache will be found in other sections. These are all designed to eliminate or correct aetiological factors, both causal and contributory.

In the acute backache with a history of injury or strain and with no radiographic or other evidence of a gross lesion, detailed examination must be postponed until the acute symptoms have subsided. Analgesics will be needed

and the patient should be at rest in bed, lying on a firm mattress in the position which gives him greatest ease; this should be sustained by pillows. Fixation of the lower back by adhesive strapping or a binder, the local application of heat (or cold compresses if there is marked local swelling or bleeding) with, later, massage and exercises to prevent contractions and adhesions, are indicated.

Treatment of chronic strain

In chronic backache due to strain, various supports—belts, braces, corsets, and plaster jackets—manipulation, physiotherapy, exercises, local procaine injections and occasionally epidural saline injections have their place. The removal of a herniated disc is often followed by dramatic improvement, but the operation must not be undertaken lightly. Such operations as division of the fascia lata, removal of long or deformed transverse processes or thickened articular facets, fusion operations on the lower lumbar spine, lumbo-sacral joints and sacro-iliac joints, and such procedures as subperiosteal stripping of the gluteus maximus or section of the pyriformis, are, except in gross disease with unequivocal indications, likely to be little practised when an unbiased assessment of their value is made on long-term results and the role of psychogenic factors in chronic backache is more generally appreciated.

Operations

REFERENCES

Copeman, W. S. C., and Ackerman, W. L. (1944). *Quart. J. Med., N.S.*, **13**, 37.
Ober, F. R. (1936). *J. Bone Jt Surg.*, **18**, 105.

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BACTERAEMIA

By E. C. B. BUTLER, F.R.C.S.
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1. DEFINITION

47.] Bacteraemia is a condition in which organisms can be cultured from the blood stream. There are two main types, transitory and persistent.

The clinical term septicaemia may be used to denote a persistent bacteraemia in which the symptoms are mainly derived from the bacteraemia itself, whereas the term pyaemia suggests a condition in which metastatic abscesses produced by the blood infection predominate. Strictly speaking the term septicaemia should be used only for a condition in which organisms actually multiply in the blood; this is seen rarely except in the terminal stages of a fatal infection such as anthrax.

2. AETIOLOGY

Specific infections

Transitory bacteraemia occurs in the early stages of certain acute infections, for example pneumonia and typhoid fever, and during operations involving infected tissues such as the removal of an infected tooth.

Endovascular foci

Persistent bacteraemia arises from an endovascular focus under the following conditions:

and the patient should be at rest in bed, lying on a firm mattress in the position which gives him greatest ease; this should be sustained by pillows. Fixation of the lower back by adhesive strapping or a binder, the local application of heat (or cold compresses if there is marked local swelling or bleeding) with, later, massage and exercises to prevent contractions and adhesions, are indicated.

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week, the percentage of cases showing lung infection would be nearly one hundred per cent.

Streptococcal.—In the haemolytic type, pyaemic abscesses are uncommon, and the characteristic necropsy findings are terminal broncho-pneumonia, enlarged septic spleen, parenchymatous degeneration of liver and kidneys and possibly purulent effusions into one or more serous cavities. Infection of the heart valves is more common in streptococcal than in staphylococcal cases.

Anaerobic streptococci may lead to abscesses in the lungs but rarely in other parts of the body.

(2) Incidence

The majority of cases of pyogenic bacteraemia are due to staphylococci or streptococci of various types. Other pyogenic organisms ocasionally produce this type of blood-stream infection but they are relatively uncommon. Before the introduction of the sulphonamides the incidence of staphylococcal and streptococcal bacteraemias was approximately the same; the majority of the latter type followed puerperal infection. Colebrook and Hare (1933) state that in a series of 100 positive blood cultures from an unselected series of puerperal infection, 60 yielded haemolytic streptococci, 38 anaerobic streptococci and 2 both types of organism.

Influence of chemotherapy

Since 1937 streptococcal bacteraemia has become increasingly rare because the infection can usually be arrested by chemotherapy before invasion of the blood stream has taken place. Between the years 1934 and 1942, 51 patients in the London Hospital died of bacteraemias associated with osteomyelitis, boils, carbuncles or infected fingers. Forty of these were due to the *Staphylococcus aureus* and only 11 to the haemolytic streptococcus.

4. CLINICAL FEATURES

The general features of bacteraemia are constant but it is convenient to describe the conditions produced by staphylococci and streptococci separately since their treatment and prognosis vary considerably.

Staphylococcal bacteraemia is characterized by its clinical variety, but for the purposes of immediate prognosis the results of quantitative blood cultures are of real value, and permit a rough classification of the cases into four groups.

5. LABORATORY METHODS

Technique

The only way of establishing the diagnosis of bacteraemia is by means of a blood culture. The following procedure should be carried out whenever possible. Blood is taken into a sterile 10 cubic centimetre syringe, and 1 cubic centimetre is run into 2–3 cubic centimetres of citrate broth or Penfold's medium, which is a salt-free broth containing 2 per cent of peptone, 2 per cent of sodium citrate and 0·1 per cent of pure saponin. The rest of the blood is cultured in the usual way. As soon as possible the sample containing one cubic centimetre of blood is mixed with melted agar at 45° to 50° C. and poured as a plate culture; it should be incubated for at least 48 hours before a final colony count is made. Contaminating colonies, if present, must be distinguished. Duplicate plates are advisable.

(i) In infective endocarditis organisms are thrown off from diseased heart valves.

(ii) In acute pyogenic infections, generally staphylococcal or streptococcal, the organisms reach the blood from an infected thrombophlebitis in a large or small vein.

(iii) In the secondary bacteraemia of non-pyogenic infections, such as typhoid fever, the blood is probably infected in the spleen and elsewhere through disintegration of cells of the reticulo-endothelial system.

This article deals chiefly with pyogenic bacteraemia and its complications.

3. PYOGENIC BACTERAEMIA

(1) Pathology

(a) *Primary focus*

Often occult

In staphylococcal infections this may be a boil or carbuncle but often no focus can be demonstrated. Streptococcal infections usually start in an area of cellulitis, the best example being pelvic infection following puerperal fever.

(b) *Mode of spread*

It has been shown by Valentine and Butler (1939) that under a primary focus small veins full of infected clot can sometimes be found; from these veins invasion of the blood stream readily occurs. The bacteraemia thus produced may be maintained either from the primary thrombosis or from further thrombosis elsewhere in the body, for example in the lungs. When a large vein such as the internal jugular is infected, it is easy to verify the source of the infection by opening the vein. The lumen is filled with pus or loose infected clot.

(c) *Secondary foci*

Sites of metastases

In staphylococcal infections these may occur anywhere in the body, the commonest sites being the lungs, bones, kidneys and soft parts. Pyaemic abscesses with haemolytic streptococcal infections are rarely found except in serous cavities, for example the pleura, peritoneum and joints. In contradistinction to staphylococcal infections, osteomyelitis and pulmonary abscesses are most unusual. Bacteraemia due to anaerobic streptococcal infection, when it occurs, frequently gives rise to multiple lung abscesses.

Anaerobic lung abscess

In all types the heart valves are sometimes infected, usually with fatal results.

(d) *Post-mortem results*

Staphylococcal.—The post-mortem results in 89 cases of acute staphylococcal osteomyelitis with fatal bacteraemia were as follows:

48	examples of	acute suppurative arthritis
75	,, ,,	lung abscesses
41	,, ,,	myocardial abscesses
10	,, ,,	endocarditis
50	,, ,,	other abscesses

The commonest lesions were lung abscesses; abscesses of the myocardium came next; actual infection of the heart valves was rare (10 per cent) but must always be borne in mind as a possible cause of persistent staphylococcal bacteraemia. In more fulminating staphylococcal cases which die within a

week, the percentage of cases showing lung infection would be nearly one hundred per cent.

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6. CLASSIFICATION

(1) Staphylococcal

(a) Group I—fulminating type

Patients in this group have a fulminating infection. Death occurs early—within 4 to 8 days. Colony counts in the blood show either high figures (500 to 1,000 per cubic centimetre) on admission or a rapid rise if the examination can be repeated.

Bacteriological criterion

This type of case is not necessarily associated with any unusual lack of immunity, and the development of the condition in any particular patient is probably a matter of chance to which neglect or maltreatment of the primary focus—for example squeezing a boil—in the early stages may often contribute. The course of this type is so fulminating that early diagnosis and treatment with penicillin is essential if the patient is to have a chance of survival.

Ten cases of this type were treated; all died. Only one of these received penicillin; necropsy revealed an active staphyloccocal endocarditis which had not responded to treatment.

(b) Group II—high colony count

The colony count in this group is above 30. The infection is less dramatic but still serious. Death may occur in from 3 to 6 weeks, giving time for the development of secondary foci, and is either due to an increasing bacteraemia or to the formation of secondary foci in vital organs which may prove fatal after the blood has become sterile. In the latter type of case death is often caused by pulmonary infection, pyopneumothorax being not uncommon according to Butler and Perry (1940).

Causes of death

Penicillin has greatly improved the prognosis of this type since the blood can be sterilized before there is time for secondary foci to become established. Fig. 1 gives the course of a fatal case treated with sulphonamides and Fig. 2 that of a patient who recovered after receiving penicillin. Of 19 examples of this group who were treated, 6 died; 5 patients received penicillin; 4 recovered and 1 died. Necropsy showed acute nephritis and pyaemic abscesses.

(c) Group III—low colony count

This group is characterized by a low colony count of less than 20. Many cases of osteomyelitis are of this type. Recovery was the rule even before the introduction of chemotherapy. Nineteen patients who were treated recovered; only 5 had received penicillin.

(d) Group IV—blood sterile

This type is characterized by the development of pyaemic abscesses while the blood remains sterile. Generally, there is a history suggesting a transient bacteraemia and presumably this must have occurred in every case. It seems that during the early bacteraemia in these cases, secondary foci are established which may remain latent for varying periods. Recovery is usual unless an abscess forms in a vital organ.

Metastatic abscesses

Quantitative blood cultures.—Since the introduction of penicillin, repeated quantitative blood cultures in staphylococcal bacteraemia have become impracticable owing to the effect of the drug on organisms which may still be reaching the blood stream. The classification which has been given of the

types of staphylococcal bacteraemia based on the intensity of the blood infection was evolved before penicillin was available, but is obviously still of value in demonstrating the initial severity of the infection. *See* Figs. 1 and 2.

If penicillin is not used, or the infecting strain is resistant, quantitative blood cultures, repeated at suitable intervals, are a valuable guide to the immediate prognosis and response to treatment.

(2) Streptococcal

(a) *Haemolytic*

The puerperal type has become very uncommon since the introduction of the sulphonamides. Blood-stream infection is generally preceded by the symptoms and signs of pelvic infection. Pelvic phlebitis may follow with subsequent invasion of the blood stream. The patient rapidly becomes very ill with high fever and rapid pulse. Pelvic abscesses and peritonitis frequently complicate the picture but metastatic lesions, apart from nephritis, are unusual. *Pelvic phlebitis*

Fulminating infection sometimes occurs, in which the blood is invaded from the beginning of the illness. These cases most often occur after a septic abortion. (*See* Abortion, Vol. I.) Clinically they resemble the first group of staphylococcal infections; the prognosis is extremely bad.

In non-puerperal haemolytic streptococcal infection, invasion of the blood may occur from an area of cellulitis anywhere in the body, from throat infections or from certain acute skin lesions, for example, erysipelas or acute lupus erythematosus. Symptoms of blood infection may be present from the start, but more commonly they arise by invasion of the blood from an area of established infection. Secondary lesions in synovial cavities are common, but abscess formation elsewhere is rare. Infection of the heart valves is more common in haemolytic streptococcal bacteraemia than in staphylococcal infections. This may explain why many cases of streptococcal bacteraemia fail to respond to treatment with sulphonamides once the blood infection has been well established. It is easier to prevent streptococcal bacteraemia than it is to cure it. The decided fall in the incidence of this disease is probably due more to the effect of chemotherapy in aborting the primary lesion than to its curative action once bacteraemia has occurred. In this respect streptococcal infections differ from those due to *Staphylococcus pyogenes*. *Aetiology* *Secondary lesions*

(b) *Anaerobic*

Bacteraemia from anaerobic streptococci has not diminished to the same extent as that due to the haemolytic variety. These organisms are often sulphonamide resistant, and occasionally penicillin resistant.

Clinically, the infection resembles that due to the haemolytic streptococcus except that lung infection frequently develops. This type of infection may start from a puerperal fever, osteomyelitis of the jaw or an area of cellulitis in the neck or lower extremities. Gas formation is not uncommon, in which case the local lesions may be confused with those due to Clostridia. *Aetiology*

Patients with diabetes seem to be particularly prone to this type of infection which usually starts as an area of infected gangrene in the leg. Rapid spread is usual and a terminal bacteraemia may occur unless the infection is checked by penicillin or amputation. *Diabetic gangrene*

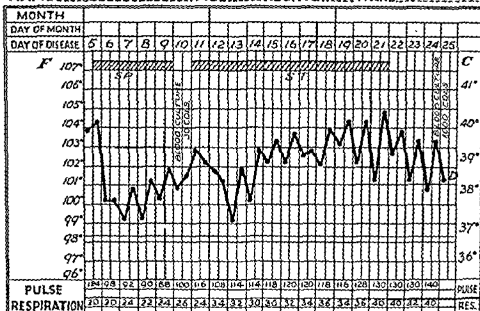


Fig. 1.—Male aged 18. Staphylococcal bacteraemia. Three weeks boil on elbow, four days pain in his arm and one day headache. On admission very ill man with few localizing signs. Blood culture—*Staphylococcus aureus*. Treatment—courses of sulphonamides given with no response. Quantitative blood cultures rose from 30 to 1,000 colonies per cubic centimetre of blood; he died three weeks after admission with signs of lung infection. There was no post-mortem examination.

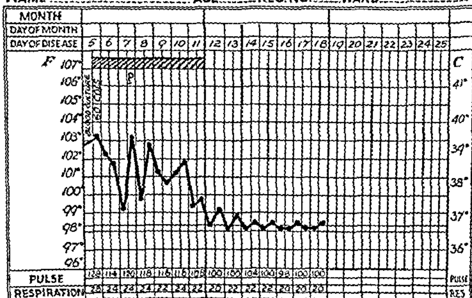


Fig. 2.—Girl aged 9. Staphylococcal bacteraemia, acute osteomyelitis of femur. Ten days boil on nose, 4 days pain in right thigh. On admission—ill but not delirious, with signs of acute infection in upper third of right femur. Blood culture—*Staphylococcus aureus*. 60 colonies per cubic centimetre of blood. Treatment—thigh and pelvis immobilized. 50,000 units of penicillin given immediately then 100,000 units every 24 hours for a further 6 days. At the end of this short course her general condition had improved and the signs in her leg had almost subsided. Later x-ray examination showed no evidence of bone infection. She has remained well since.

7. DIAGNOSIS

Acute pyogenic bacteraemia is often difficult to diagnose but the condition should be suspected in the presence of the following symptoms and signs, especially when they are associated with an active pyogenic focus somewhere in the body.

Onset.—This is frequently sudden, accompanied by headache, shivering and repeated vomiting.

Temperature.—This remains high and rarely drops to normal in the 24 hours. A swinging temperature indicates a localized lesion rather than a bacteraemia.

Pulse.—The pulse rate is raised.

Respiratory rate.—A persistent respiratory rate of over 30 is often a sign of early pulmonary infection; this should be regarded as a grave sign despite the absence of definite auscultatory signs in the lungs.

Delirium.—This is often present in severe cases, but is not necessarily associated with a high colony count. It may be present in cases of toxaemia with a negative blood culture.

Rigors.—A single rigor often ushers in the disease. Repeated rigors are uncommon in all types of pyogenic bacteraemia unless infected emboli are being shot off from a large vein. In these cases a diagnostic blood culture should be taken during or immediately after a rigor as the blood may become sterile between the attacks.

Splenomegaly

General examination.—In cases of streptococcal infection, enlargement of the spleen, petechiae and cardiac murmurs are particularly important. Staphylococcal infections do not generally cause these signs, but occasionally a pustular skin eruption occurs which has been mistaken for smallpox.

8. DIFFERENTIAL DIAGNOSIS

Toxaemia

Toxaemia from acute pyogenic infections may closely simulate bacteraemia, especially if there is an undrained focus of infection under tension. Patients with such a condition are severely ill with high fever, rapid pulse and sometimes delirium. An initial rigor may occur. Response to surgical drainage and chemotherapy is usually dramatic. A blood culture is often required to exclude a bacteraemia.

Rheumatic fever

Many cases of staphylococcal bacteraemia with acute osteomyelitis have been diagnosed as rheumatic fever; local bone pain may be mistaken for arthritis especially in the presence of a "sympathetic" joint effusion. Patients with bacteraemia often complain of pain in various joints which may vary in intensity from day to day as in rheumatic fever. A careful history and examination will generally make the diagnosis clear; delirium and rigors are almost unknown in rheumatic fever but are characteristic of bacteraemia.

The therapeutic test with salicylates should not be used to decide an uncertain diagnosis, as valuable time may be lost should the diagnosis of rheumatic fever be incorrect.

Any child suffering from high fever, delirium and bone pain should receive immediate treatment with penicillin without awaiting the result of a blood culture or response to salicylates.

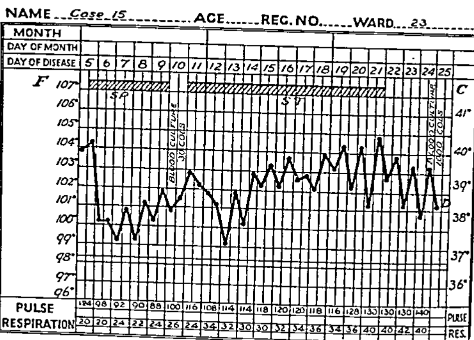


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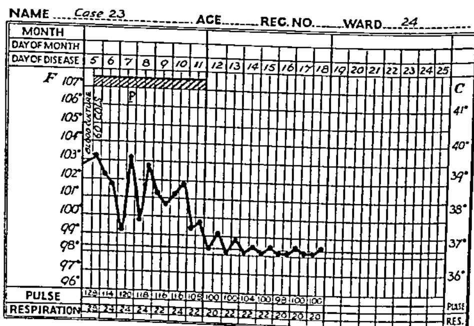


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Specific fevers

The early stages of many specific fevers and non-pyogenic infections may give a picture resembling bacteraemia, but the typical lesions of the individual infection generally manifest themselves before long. In doubtful cases the leucocyte count and blood culture are valuable aids to diagnosis.

9. TREATMENT

Objects

The treatment of pyogenic bacteraemia should be directed towards (1) the primary focus, (2) the bacteraemia, (3) secondary foci, (4) the toxaemia and (5) general measures.

(1) Primary focus

In streptococcal cases the primary lesion is generally an area of cellulitis which is easily demonstrated clinically. The inflamed part, if possible, should be completely immobilized. Absolute rest is essential for haemolytic streptococcal lesions until all signs of the acute phase have passed. Movement instituted too early may readily cause an exacerbation of the local and systemic infection. Surgical treatment is never needed except to drain an abscess or, rarely, to relieve tension.

Immobilization

Drainage

The primary site of a staphylococcal bacteraemia is often difficult to demonstrate, as a small skin lesion may be the starting-point of a severe blood infection. Complete excision of such foci has been shown to be justifiable by Butler and Valentine (1943) in cases with a high bacteraemia in order to eliminate a possible source of the blood infection. In all cases pus should be aspirated or drained if under tension.

Excision

Since penicillin was introduced, treatment of a small primary focus is perhaps of less vital importance, but it remains desirable.

Venous ligation

Ligation of a large infected vein is always justifiable. The response to this operation may be dramatic; rigors cease and the blood rapidly becomes sterile since the ligature effectively prevents the infected clot from being thrown into the blood stream. Ligation of the internal saphenous vein in cases of purulent infection with pyaemia is a good example of this mode of treatment.

Bacterial endocarditis

In a different group of cases, ligation of a patent ductus arteriosus has produced dramatic results in the treatment of bacterial endocarditis. Ligation of a small vein, such as the angular vein in facial infections in the hope of preventing cavernous sinus thrombosis, has no practical value. The anatomy of the facial veins is so complex that ligation of one of them is inadequate and is therefore bad surgery. In two consecutive cases of cavernous sinus thrombosis the infection was found at necropsy to have passed from inside the nose via veins which had no relation to the small uninfected angular vein.

(2) Bacteraemia

Penicillin.—The introduction of this drug has materially altered the prognosis and simplified the treatment of bacteraemia. Treatment should be instituted as soon as the diagnosis is clinically certain, without waiting for the result of a blood culture.

Dosage

In adults the dose recommended at the present time is a minimum of 100,000 units in 24 hours; in severe cases the dose should be doubled or trebled. Administration is usually by a continuous intramuscular drip or by repeated intramuscular injections every 3 hours.

Treatment should last for at least 10 days; in severe cases patients require the drug for 3 weeks or longer. If penicillin is stopped too soon, relapses may occur with recrudescence of the bacteraemia.

Duration of treatment

At present the dose for children varies from 25,000 units daily in a small baby up to adult doses after puberty. Repeated intramuscular injections are used in babies, and the total volume of fluid reduced in older children receiving the intramuscular drip in order to prevent oedema of the legs. In future it may well be that the methods and dosage here described will be greatly modified.

In early cases before the formation of secondary foci, clinical improvement, as shown by a fall in the temperature and pulse and return of appetite, may be rapid. In later cases the presence of an undrained focus somewhere in the body may delay clinical improvement until the focus is drained even if the blood has become sterile.

If acute pyogenic endocarditis supervenes the prognosis is much worse, and the response to penicillin may be disappointing, although successful cases have already been reported by Dolphin and Cruickshank (1945).

The temperature may not settle until the penicillin has been stopped, because irregular pyrexia is still common with certain samples of the drug. This phenomenon may disappear when purer preparations are available. If irregular pyrexia continues after penicillin therapy has ceased it is usually due to the presence of some undrained focus in the body.

Heparin.—This drug inhibits the formation of intravascular thrombosis. Using a combination of heparin with sulphathiazole, Lyons (1942) treated cases of staphylococcal bacteraemia successfully, and lately heparin has been used with penicillin in the treatment of malignant endocarditis by Loewe (1945). The daily dose of penicillin varied with the sensitivity of the causative streptococcus (40,000 to 1,000,000 units) and the total amount given was between 167,000 and 48,900,000 units. Loewe reports 54 cases with 14 deaths and 40 successes, 37 of the latter being well up to 15 months after treatment.

Combined treatment

Three hundred milligrams of heparin are given subcutaneously in a gelatin medium every second or third day, the dose being determined by estimations of the coagulation time, which should be kept between 30 and 60 minutes. Owing to the danger of cerebral haemorrhage heparin should not be used unless laboratory facilities are adequate for such estimations. The real place of heparin in the treatment of endocarditis has yet to be determined.

Dosage

Equally promising results, however, have been reported by Christie (1946) using 500,000 units of penicillin daily for 6–8 weeks, without the aid of heparin.

Sulphonamides.—Sulphathiazole is generally accepted as the most suitable of the sulphonamides for use in pyogenic bacteraemia. Others which can be employed include sulphadiazine and Sulphamezathine.

The results achieved with these drugs do not equal those obtained with penicillin, but they should always be given in the absence of the latter drug. The sensitivity of the causative organism must be borne in mind. The dose must be sufficient to obtain an adequate concentration in the blood, that is at least 2 grammes every 4 hours for severe cases, with a total dosage of about 70 grammes. The leucocyte count should be watched to exclude a dangerous leucopenia.

Leucopenia

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The urine should be kept alkaline with potassium citrate and plenty of fluids given orally to combat the danger of deposition of sulphonamide crystals in the urinary tract. Gross diminution of the urinary output coupled with the presence of many sulphonamide crystals in the urine are indications that the drug should be stopped at once.

Oliguria

If no clinical improvement follows a full course of one of these drugs, it is harmful to start another course. The sulphonamides are poisonous and should be administered only if their action is beneficial.

(3) Secondary foci

Patients suffering from pyogenic bacteraemia are liable to develop metastatic lesions in any part of the body. Sometimes these foci overshadow the bacteraemia, for example in acute osteomyelitis; in other cases they develop insidiously in the soft parts or lungs. During the acute phase bone infection needs surgical intervention only if the symptoms and signs of intra-osseous tension are present; this will be shown by persistent bone pain and fever despite adequate treatment with penicillin. In many cases no operation is required as the infected bone is sterilized by the drug alone.

Indication for surgery

Lung

Pulmonary infections should be suspected if there is a rapid respiration rate, and must be watched for with the aid of repeated x-ray examinations. Fortunately, they respond well to chemotherapy. Pyopneumothorax, if it occurs, should be treated by repeated aspiration, with injection of penicillin solution into the pleural cavity according to Butler, Perry and Valentine (1944). Rib resection may be needed after the pleural effusion has become sterile especially in staphylococcal infections.

Rib resection

Metastatic lesions in other parts of the body usually develop gradually. They should be drained by an appropriate incision. Secondary foci in streptococcal infections usually yield to aspiration, with the injection of penicillin solution into the infected cavity. Drainage may be required if the pus becomes too thick to pass through a needle.

(4) Toxaemia

Toxaemia is never fatal in pyogenic bacteraemia. In streptococcal infections no special treatment is required. Streptococcal antitoxin has been discarded since the introduction of the sulphonamides.

Leucocidin

Antitoxin

In staphylococcal infections the leucocidin is probably the most important toxin. Valentine and Butler (1939) have shown that staphylococcal antitoxin with a high antileucocidin titre has a beneficial effect in acute staphylococcal infections during the first few days of the disease. Bacteraemia, however, is not affected by serotherapy. The antitoxin should be given intravenously, and the dangers of anaphylaxis must not be forgotten. Since penicillin was introduced serotherapy has been discontinued.

(5) General measures

Fluid replacement

Nourishment.—Plenty of fluids must be given to replace the extensive loss by sweating and other causes. Glucose lemonade is well tolerated. Solid food is not required and cannot be digested. Directly the patient's appetite returns the diet may be rapidly increased.

Transfusion

Anaemia.—Secondary anaemia often develops quickly. Small repeated blood transfusions of not more than one pint are often very beneficial, and during

convalescence iron should be given. Patients who have recovered from bacteraemia require, as a rule, a long convalescence with fresh air and sunlight. In the winter general ultra-violet irradiation is helpful provided that the dose is carefully regulated by a specialist in physical medicine.

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[References to other titles are given under Bacteraemia in the Index Volume. The subject of Bacteraemia is also dealt with under the heading of Septicaemia and Bacteriaemia in the *British Encyclopaedia of Medical Practice* (1939), Vol. 2, p. 76.]

BACTERIOLOGY

By E. T. C. SPOONER, M.D.
Fellow, Clare College, Cambridge

1. GENERAL PROPERTIES OF BACTERIA

Surface antigens

48.] Most bacteria conform to a general chemical-morphological pattern. The bacterial cell measures 0·5 to 2·0 by 0·8 to 7·0μ. The surface of the cell is usually coated with a water-soluble antigenic gum, a carbohydrate-lipoid-protein substance secreted during active growth, which makes the cell sticky so that it adheres to any surface it touches. The gum may be sufficiently abundant to form a visible capsule. The surface antigens of pyogenic cocci are not poisonous but confer virulence by protecting the cocci from phagocytosis. Their varied antigenic specificity makes possible both classification and the recognition of strains. The surface antigens of Gram-negative bacilli, or O antigens, are also useful for classification; they contribute to virulence by preventing phagocytosis and because many of them are the endotoxins of the bacilli.

Life history

The life history of bacteria is simple. If food and water, temperature, gas environment and acidity are adequate, a bacterial cell increases in size to a limit peculiar to the species, and then splits into two smaller units which in turn grow and divide. Under optimal conditions most bacteria, other than the *Mycobacteria*, can multiply at intervals of 15 or 20 minutes. One cell can generate several millions in a few hours. Obviously multiplication at this rate cannot continue for long; food is soon exhausted and poisonous metabolites accumulate, so that reproduction slows and ceases, until dispersal of the colony or accession of fresh culture medium restores optimal conditions.

Multiplication

Bacteria rarely grow and multiply without restraint for a significant time. They may do so for a few hours in cultures and sometimes in a wound such

as a burn. A fulminant septicaemia due to *Streptococcus pyogenes* or *Clostridium welchii* may indicate unrestrained "logarithmic" growth, but infections of this kind are rare and depend upon the chance entry of fully virulent micro-organisms in the right growth phase into a completely susceptible body. It is more usual for invading bacteria to meet opposition or to exhaust a limited local food supply so that continued rapid proliferation stops.

Colony formation in the body

Occasionally invading bacteria produce coherent colonies similar to those on an agar plate culture. Colonies of staphylococci may be seen in sections of hair follicles. Smears from the lining of the mouth or from sputum may contain colonial clumps. Bacteria in vegetations of endocarditis, protected by fibrin through which nutriment can diffuse, may form colonies which are macroscopically visible in stained sections. Similarly, on an infected wound surface microcolonies may form in the fibrin, so that samples taken by capillary tube from different parts of the wound yield different kinds of bacteria or none at all. Invading bacteria are usually scattered by movements of cells and fluid, and have little chance of colony formation or unrestrained multiplication.

"Resting" bacteria

In old cultures, the average cell size is smaller, and multiplication ceases. The bacteria enter a "resting" phase in which they show little activity of any kind; they no longer grow or divide, and their metabolism falls to a minimum. In this state, they may be more resistant to heat and chemical disinfectants, but are usually more susceptible to phagocytosis. Capsules, if present earlier, dissolve away. Spore-producing species may sporulate. In the body bacteria probably seldom enter such a "resting" phase, for those not actively growing are removed by phagocytes. Spores, which may survive inside phagocytes, are an exception and may lie dormant in living tissues for years.

The "lag phase"

If resting bacteria are transferred to conditions optimal for growth, they do not immediately multiply; for a time the cells mobilize their biochemistry and commence to metabolize and to grow. The duration of the "lag phase" depends partly upon the physical and chemical conditions of the new environment, partly upon the growth phase of the parent culture. The nearer the parent culture is to a phase of active multiplication, the shorter the lag. Subculture during logarithmic growth may practically abolish lag.

Septicaemia

If a pathologist making a post-mortem examination pricks his finger and inoculates himself with haemolytic streptococci which are actively multiplying in the cadaver, they may be capable of immediate proliferation in their new host, and a fatal septicaemia may develop in a few hours.

State of normal body flora

Most bacteria on body surfaces and in the gut or in wounds are either dead or resting, because conditions favouring multiplication are local and evanescent. Faeces, for example, are largely composed of dead bacteria, as is pus which has lain for some weeks within a closed plaster. Such pus is chiefly composed of bacteria, most of them dead, which in time degenerate to an amorphous cream.

Dispersal

Like plants and animals, bacteria and viruses must travel to new feeding grounds if their species are to survive. Their power to travel is often remarkable. Influenza in 1918 to 1919, with no inherent means of locomotion, covered the Earth in less than a year. The plague bacillus and yellow fever virus, like protozoon and worm parasites, travel in intermediate hosts such as fleas and mosquitoes. Others, like *Treponema pallidum*, depend upon direct

contact between hosts. Knowledge of the mode of spread of intestinal infections in polluted water and food made possible the control of cholera and enteric fever even before the bacteria causing them were known. Surgeons are more concerned with the pyogenic cocci and Gram-negative bacilli which are spread by contact and in the air.

"Stickiness"

The "stickiness" of bacterial surface gums is probably important in this context. Bacteria adhere readily to any surface they touch, a fact exploited in making film preparations on microscope slides or in using a cotton-wool swab to obtain a sample for culture, or a cotton-wool plug as an air filter in a culture tube.

Perhaps the most important corollary to the idea of bacterial stickiness is that bacteria will not blow about in the air, except on dust particles to which they adhere. A bacteriologist can safely open his plate and tube cultures, even in a draught, without letting any of the contained bacteria escape. He can transfer bacteria on wires or swabs without fear that they will drop off into the air. There is, however, another corollary—that any object touching a contaminated surface may gather bacteria from it and deposit them on any other surfaces to which they can adhere. It is a matter of common domestic experience that sticky materials can contaminate numerous and unexpected surfaces if they escape from their proper containers.

Wet and dry swabs

Damp objects pick up bacteria and deposit them more readily than do dry ones. If two cotton-wool swabs, one dry and the other moistened with sterile saline, are rubbed over comparable areas of skin and then over agar plates, the plate inoculated from the moist swab will produce many more colonies than will the other. Wet fingers act like wet swabs.

Because their surfaces are hydrophilic, bacteria adhering to a surface are easily washed off it by water, a reflection which should be a warning against doing minor surgery and dressings with wet hands.

Effect of drying on bacteria

Bacteria are very tolerant of drying. Delicate organisms such as the meningococcus, which easily die in cultures, remain viable for years if rapidly dried *in vacuo* from the frozen state, suspended in some protein-containing fluid such as serum-water. The pyogenic cocci withstand drying at room temperature in air, and may remain viable for months in dry dust. Spores are still more resistant. Collections of stock cultures are often kept in the dry state.

2. BACTERIOLOGY OF DUST

Lister recognized dusty air in theatres and wards as a threat to wounds. Tyndall, in classical experiments on spontaneous generation, showed that dust-free (optically clean) air did not contaminate media exposed to it. Air in theatres and wards is not dust-free, and always carries bacteria on dust particles. Most of these are non-pathogenic and come from plants, soil, and the throats, skin and clothes of man. Lister attempted to kill air bacteria with the carbolic spray, but later, realizing that most of them are non-pathogenic, he gave up the spray.

Pathogens in dust

Important pathogenic bacteria in dust are *Streptococcus pyogenes*, *Staphylococcus pyogenes*, *Corynebacterium diphtheriae* and *Clostridium welchii*. Of these *Str. pyogenes* has been most intensively studied. It comes from the throats of carriers who expel it in droplets when they cough, sneeze or talk.

Bourdillon and Lidwell (1941) have shown that on sneezing, droplets of visible size are expelled with a velocity up to 150 feet per second, to a distance up to 5 feet. Hare (1940) has ingeniously studied the trajectories and bacterial content of these droplets. Big drops fall almost vertically, only the smaller ones reaching a distance of more than a foot or two measured horizontally. The number of haemolytic streptococci expelled in droplets is not so great as might be expected, but is enough to make the throat of a carrier a major surgical hazard. The droplets fall either on to clothes or bedding, or on to the floor. Small drops dry before they reach the ground; large ones dry where they fall, leaving nuclei of solid matter containing the bacteria.

Clothes and bed clothes

When clothes or bed-clothes are shaken, dust from them carries bacteria into the air. Bedmaking especially, or sweeping, multiplies the bacterial content of the air nearly a thousandfold. Thomas and van den Ende (1941) found 3 to 14 colony-producing haemolytic streptococci per cubic foot of air in an oto-rhinological ward, and near a bed which was being made, 2,500 such streptococci per cubic foot.

The "slit sampler"

Air bacteria are counted with the "slit sampler" of Bourdillon, Lidwell and Thomas (1941), a machine which sucks measured volumes of air through a narrow slit placed radially to and just above the surface of a revolving agar plate. Over 90 per cent of the bacteria in the air are deposited on the agar; those which the medium suits grow into countable colonies. For haemolytic streptococci, Garrod's gentian violet agar is used.

Number per cubic foot of air

Published counts of haemolytic streptococci per cubic foot of air vary from 0 to about 40 during quiet periods, with much greater numbers during periods of ward activity such as bedmaking. Total bacterial counts corresponding to these figures are from 1 to 10 thousand times as great. Figures for *Staph. pyogenes* and *Coryn. diphtheriae* are not available.

Fate of inhaled streptococci

A man at rest passes about 12 cubic feet of air over his respiratory mucosa per hour, and the respiratory passages retain up to 90 per cent of inhaled bacteria. Every patient in a ward will inhale some haemolytic streptococci each day; during ward activity, each patient must inhale several hundreds every hour. This risk is greatest in scarlet fever and ear, nose and throat wards, in which the air streptococci are most numerous.

The throat carrier rate for haemolytic streptococci in a ward is seldom more than 20 per cent. Presumably most dust streptococci which form colonies on blood agar cannot survive in the respiratory passages. The extent to which they can colonize wounds is unknown. Wounds do not breathe and are therefore exposed to a smaller risk than are respiratory passages—a risk which is more accurately measured by exposing culture plates than by using a slit sampler.

Bacteria falling from air

The slit sampler measures the number of bacteria per cubic foot of air; the exposed plate measures the smaller number falling on to unit area in unit time. In one ward in which the throat carrier rate was 16 to 28 per cent and most wounds were streptococcus infected, roughly 6 colony-producing streptococci fell per square foot per hour. In another ward, corresponding figures were 7 and 10. (References to other methods of sampling dust bacteria are given by Bourdillon, Lidwell and Thomas, 1941.)

Haemolytic streptococci per gramme

Floor dust is more heavily contaminated than dust from walls and window sills. Garrod (1944) has produced evidence that diffuse daylight, coming

through glass, is to a certain extent lethal for dust streptococci. The dust from some wards contains no demonstrable haemolytic streptococci, but Thomas and van den Ende found dust from an ear, nose and throat ward which contained 20 millions per gramme.

Diphtheria bacilli

Crosbie and Wright (1941) found abundant diphtheria bacilli in the dust of diphtheria wards, but not elsewhere. They can survive and remain virulent in dust for months.

Control

Recently, attempts have been made to reduce the bacteria in ward air by treating floors, clothes and bedding with oil to prevent dust from rising. Properly executed, these measures are effective. Reference may be made to van den Ende, Lush and Edward (1940); Thomas and van den Ende (1941); van den Ende and Thomas (1941); Crosbie and Wright (1941); Wright, Cruikshank and Gunn (1944) and Anderson, Buchanan and MacPartland (1944). Wooden floors are most suitable for oiling. Oiling properly done renders the floor less slippery for leather, but more so for rubber, and is therefore unpopular in orthopaedic wards. The oil treatment of bedding has been simplified by Harwood, Powney and Edwards (1944) and is practicable in any well-equipped laundry.

Probably the most effective means of controlling ward dust would be central built-in vacuum cleaning as used in hotels. The traditional brush and duster, with much labour, remove only a fraction of the dust and infect the ward atmosphere for an hour or so after use, circulating dust to and fro from beds to floor and floor to beds indefinitely.

Although the dust hazard can be estimated in terms of bacteria inhaled per hour or falling on to unit area in unit time, its true danger is still unknown, for we do not know what dust bacteria can do in the body. The only reasonable attitude is to treat all dust "pathogens" as dangerous, as they probably are, remembering that the risk is small to exposed wounds, greater to respiratory passages, but anything which increases the respiratory carrier rate also increases the main reservoir whence wounds are infected by droplet and contact spread.

Operating theatres

The air of operating theatres is much safer than that of most wards, and in fact presents a very small risk indeed to surgery, according to Rice, Weed and Raidt (1941). In the United States much work has been done on the control of air bacteria by means of ultra-violet light screens. A useful review of this work, and of many other matters relating to the prevention of cross-infection, is to be found in *Micrurgical and Germ-Free Techniques* by Reyniers (1943).

3. DISINFECTION

Bacterial death

There is a steady mortality in any bacterial population, even during the phases of most active growth. In old cultures mortality outstrips multiplication, so that the culture as a whole ultimately dies. The viable bacteria remaining in an old culture may, individually, resist disinfection better than younger cells. Artificial disinfection, whether by heat or by chemicals, must always aim at destroying these highly resistant individuals, even though their numbers be small. For this reason successful disinfection methods allow a big margin of safety. The elimination of populations, including those of bacteria, is more than a piecemeal destruction of individuals: "slaughtering-out" policies are

seldom successful, because enough individuals usually escape to multiply afresh.

Disinfection by heat, properly carried out, is always easier to control and more efficient than chemical disinfection, and should be used in surgery whenever possible. There is not space in this section to discuss the practice of disinfection; useful practical information may be obtained in the Medical Research Council *War Memoranda* Nos. 6, 11 and 15, and in a paper by Garrod and Keynes (1937). When chemical disinfectants have to be used, certain principles must be observed.

(1) Practical principles

(i) The disinfectant must be used at a sufficiently high concentration. Dilution rapidly removes the effect of many disinfectants.

(ii) No disinfectant at a reasonable working concentration acts instantaneously. The time taken to kill increases with dilution and decreases with rises in temperature.

(iii) Different disinfectants are more effective against different bacteria. Generally, these specific differences do not affect usage, except in the case of disinfectants applied to the body.

(iv) Disinfectants vary in the extent to which they are neutralized by dirt and protein matter. The best guide to this property is the consideration of whether a disinfectant kills by combining with bacterial proteins. Those that act in this way are more or less inert in the presence of excess protein, such as blood or pus. One great merit of modern chemotherapeutic drugs is that they do not combine with protein.

(2) Aerial disinfection

Disinfectants are usually chemicals which act in watery solution. Disinfection of air presents special problems which are receiving much attention by those concerned with the control of respiratory infections. At present, however, aerial disinfectants are not of great importance in surgery. If it is considered advisable to disinfect the air of a ward, the only satisfactory procedure is to disinfect the dust in the ward at the same time. For this purpose, formalin fumigation, as recommended by Fry (1941), is very satisfactory. It is desirable that all surgical wards should be treated with formalin by this method from time to time.

4. PYOGENIC COCCI

The pyogenic cocci interfere with surgery more than do any other bacteria; they also produce many of the pathological states which require surgical treatment. The most important are *Streptococcus haemolyticus* and *Staphylococcus pyogenes*.

Chemotherapy has gone far to deprive haemolytic streptococci of their dangers, but they still rank highest among bacteria affecting surgery. Before the introduction of serological classification, the surest laboratory guide to the virulence of a streptococcus for man was haemolysin production. Griffith (1934) differentiated about 30 agglutinative types among haemolytic streptococci isolated from human lesions and throats. Streptococci of any Griffith type may cause any kind of streptococcal disease. About 60 per cent of haemolytic streptococci are typable by Griffith's method. Untypable *Griffith's types*

strains may be pathogenic, but Griffith found that virulent epidemic strains are more easily typed than are sporadic ones. Griffith's method of typing enables a bacteriologist to follow a strain of streptococci as it passes from wound to wound, from throat to wound or from wound to throat.

Lancefield's groups

At about the same time, Lancefield (1933) classified haemolytic streptococci by another method, extracting them with hot hydrochloric acid and using the extracts as antigens in precipitation tests against antisera from immunized rabbits. By this method, most strains of human origin fall into one antigenic group, called Group A. Streptococci from cattle, including those of bovine mastitis, form a Group B. Except in rare cases of puerperal infection, according to Fry (1938), Group B streptococci are not pathogenic to man; they are seldom found in throats. Group C and Group G streptococci are found occasionally in human throats, noses and lesions. Group C streptococci are occasionally associated with scarlet fever.

The specific antigen of Group D is shared by many non-haemolytic streptococci and is characteristic of faecal streptococci, which are not pathogenic except in bacterial endocarditis and in some localized lesions.

Str. pyogenes

Most of Griffith's agglutinative types belong to Lancefield's Group A, a few to Group C. It is not inappropriate to use the name *Str. pyogenes* for these groups which may be pathogenic to man. Between 15 and 20 per cent of strains of *Str. pyogenes* are micro-aerophilic in the sense that they will not grow aerobically on first isolation, but become aerobic after a few subcultures.

Oxygen requirements

Str. pyogenes is the invariable cause of erysipelas, streptococcal septicaemia and scarlet fever, and a frequent cause, but not the only one, of puerperal infection, tonsillitis, wound infection with delayed healing, failure of skin grafts, empyema, pneumonia and various other diseases, many of which constitute "complications" of hospital treatment as well as occurring spontaneously outside. *Str. pyogenes* is also frequent in normal throats and wounds in which it seems to do little or no damage.

Diseases caused by Str. pyogenes

We do not know why streptococcal infection sometimes produces disease and at other times does not. Probably much depends upon the local and general resistance of the patient, neither of which can we measure. One strain of streptococci of recognizable type may do no apparent damage in some patients, while making others in the same ward seriously ill, or delaying their recovery.

Variable resistance of patients

Strains probably differ in their inherent virulence, but there is no satisfactory method of directly measuring virulence for man. Occasionally one strain may travel round a ward producing very similar lesions, such as otorrhoea, in several patients. Epidemics of scarlet fever or streptococcal sore throat are usually due to one type of *Str. pyogenes*, even though streptococci of other types are present at the time in the community at risk, but are taking no part in the epidemic. In such epidemics, serological typing may allow a small number of carriers of the epidemic type to be segregated, when the isolation of all streptococcal carriers might be impracticable.

Variable virulence

The portal of entry is an important determinant of streptococcal disease. When a virulent streptococcus enters a clean wound at operation, rapidly fatal infection may follow. Miles and others (1940) report such an incident when theatre infections due to a Type 11 streptococcus occurred in two

Portal of entry

patients operated upon on the same day in the same theatre by the same team. One died in a few days from secondary haemorrhage; the other suppurated but was not made seriously ill. A nurse in the theatre team was an abundant throat carrier of the same type of streptococcus.

Meleny and Whipple (1945) state that infections developing in wounds during the first five days are more serious than those developing in the second five days. Cruikshank (1940) and Coller and Valk (1940) report similar observations. Probably granulation tissue in a wound can block the spread of infection to deeper tissues. Barnes and Trueta (1941) draw attention to this property of granulation tissue. The liability of scarlet fever to follow tonsillectomy, according to Okell and Elliott (1936), also indicates the vulnerability of wounds unprotected by granulation tissue. *Granulation-tissue barrier*

Granulation tissue may limit the spread of infection in the reverse direction. The author failed repeatedly to isolate haemolytic streptococci from a wound completely surrounded by erysipelas which had started in a second wound 16 inches distant, from which haemolytic streptococci were obtained.

In wounds protected by granulation tissue, *Str. pyogenes* may delay healing and prevent the "taking" of Thiersch grafts unless adequate chemotherapeutic measures are taken to control it. *Str. pyogenes* is of special importance in burns (Colebrook, 1945).

The only reservoirs of *Str. pyogenes* are lesions such as wounds and the human upper respiratory tract. From these, it reaches the dust of rooms, clothing, bed-clothes and other objects which may carry it to fresh hosts. *Reservoirs*

The frequency of *Str. pyogenes* in throats varies from 2 to about 30 per cent. Frequencies of 10 or 15 per cent are usual in closed communities. The throat of a carrier may or may not be clinically inflamed. It may yield very few colonies on culture, or an almost pure culture. Some throat carriers are also nasal carriers. Willitts and Hare (1941) found a high throat carrier rate among those with wounds infected with streptococci of similar type. Spooner (1941) found that 10 out of 15 patients with burns of the face became profuse throat carriers. Carrier rates are highest in the winter. *Throat*

Colebrook (1935) demonstrated the importance of throat carriers in connexion with puerperal sepsis. Okell and Elliott (1936) showed that haemolytic streptococci spread easily among throats and lesions in oto-rhinological wards. The relation of streptococcal throat carriers to wound and theatre infection has been emphasized by Miles and others (1940), Williams and others (1944), Hare (1941), Willitts and Hare (1941) and others. (*See* also Medical Research Council *War Memoranda* Nos. 6 and 11.)

Str. pyogenes is not usually found on the skin except near a wound infected with it, or on the fingers of a respiratory carrier. Colebrook, Maxted and Johns (1935) examined 180 pairs of hands of factory and hospital workers and found 8 strains of *Str. pyogenes* on them. Hare (1941) recovered one strain only from the hands of 248 subjects. The author's experience is that they are more common on finger tips, especially those of throat carriers. *Skin*

Colebrook (1930), Arnold and others (1930) and Burtenshaw (1938) state that haemolytic streptococci placed on the skin die out rapidly. The mechanism of this bactericidal action of skin is unknown. It is impaired by dirt, and is in any case not powerful enough to be trusted to make skin, and especially that of fingers, safe. *Streptocidal power of skin*

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In vivo, antitoxin confers some immunity on experimental animals, but protection is incomplete. Immunized rabbits are immune to the dermotoxin, but a certain number of them develop local abscesses in internal organs after an intravenous injection of living staphylococci (Smith, 1937). *Immunity*

The amount of staphylococcal antitoxin in normal human blood is between about 3 units per millilitre of serum and quantities too small to detect. The average normal value is about 0·75 unit per millilitre of serum; titres of more than 2 units per millilitre are rare in normal subjects and in those suffering from superficial staphylococcal lesions, but more common in those suffering from chronic and deep-seated disease like osteomyelitis.

Attempts to control staphylococcal disease in man by raising antitoxic immunity have given inconsistent results. Dolman (1933), Whitby (1936), Ramon (1936) and Mercier (1937) have all reported very good results from the treatment of superficial and other staphylococcal disease with toxoid. Panton (1936) and Klaber (1936) have not been so successful. Treatment with toxoid is occasionally followed by an exacerbation of the disease.

Treatment with antitoxin has been equally uncertain (Editorial, *Lancet*, 1934).

Vaccine therapy also has received very varying success. Downie (1937) has shown that any immunizing power in a staphylococcal vaccine can be accounted for by the toxin or toxoid which it contains.

Much depends upon our conception of the pathogenesis of staphylococcal disease. Toxin probably plays a big part but other factors may operate. The work of Panton and Valentine (1929) and of many subsequent observers suggests that staphylococcal lesions are partly allergic, but the relative importance of toxin and allergy remains uncertain. *Pathogenesis and allergy*

No immunological treatment and no chemotherapeutic treatment is likely to succeed unless accompanied by adequate surgery.

The main reservoir of *Staph. pyogenes* is the human nose. Miles, Williams and Clayton-Cooper (1944) report a nasal carrier rate between 19 per cent and 65 per cent at different times of the year, the mean being between 40 and 50 per cent. These figures agree with those of other workers. The nasal carrier rate is said to be higher among those suffering from staphylococcal lesions than among normal people (Viertheiler, 1940). The nasal carrier rate among infants in maternity homes is usually higher than that among adults. *Nasal carriers*

Staph. pyogenes is commonly found in mothers' milk, sometimes in very large numbers. A high milk count is not usually associated with breast abscess or other form of ill health in either mother or child. *Mothers' milk*

Staph. pyogenes is also commonly carried on the skin. Skin carrier rates vary between 5 and 20 per cent, the higher figure being more usual with respect to the "transient" skin flora, the lower with respect to those in whom the staphylococcus is in the hair follicles and sebaceous glands, the true, persistent carriers whom even "scrubbing up" and the use of rubber gloves will not make completely safe (Devenish and Miles, 1939). Most skin carriers are nasal carriers as well. *Skin carriers*

In view of the high frequency of carriers, it is not surprising that *Staph. pyogenes* is the commonest pathogenic microbe in wounds. Williams and Miles (1945) state that about one-third of small wounds infected with *Staph. pyogenes* show clinical sepsis. The clinical state of the wound is not related to *Wounds*

Anaerobic streptococci

In addition to *Str. pyogenes*, anaerobic streptococci are sometimes isolated from lesions. Fleming (1915) mentions them as occurring in war wounds. In 1933 Colebrook and Hare revealed their importance in puerperal sepsis and described forty strains isolated from the blood of women suffering from that condition. The normal habitat of anaerobic streptococci is the vagina. White (1933) found them in approximately 30 per cent of normal vaginas. Attempts to isolate them from faeces and from body surfaces other than the vagina have usually failed. They do not possess much invasive power; probably they became pathogenic only when they can multiply freely in dead or diseased tissue, as in some puerperal uteri.

Haemolytic and non-haemolytic strains are described. The haemolytic strains are distinct from *Str. pyogenes*, with micro-aerophilic strains of which they are sometimes confused. Colebrook and Hare (1933) differentiated four different kinds of anaerobic streptococcus, but little is known of their general bacteriology (Sandusky and others, 1942).

Meleney's "burrowing" lesion

Meleney (1933) has described a progressive gangrene of the skin associated with anaerobic streptococci, occurring after operations or around accidental skin abrasions. These lesions are shallow and "burrowing", with undermined edges and a purple surrounding skin area, and are slowly progressive in spite of local treatment.

Anaerobic streptococcal myositis

In war wounds, MacLennan (1943, 1944) has described anaerobic streptococcal myositis which may be mistaken clinically for gas gangrene. Some strains of anaerobic streptococci are sensitive to penicillin.

Staph. pyogenes

Second in importance to *Str. pyogenes* among the pyogenic cocci is *Staph. pyogenes*. The name *Staph. pyogenes* omits reference to pigment, and is appropriate to all pus-producing staphylococci. The property most closely correlated with pus production is the power to clot citrated human plasma, according to Cruikshank (1937). Staphylococci which do this produce a

Coagulase

coagulase during their growth. Coagulase reacts with an activator present in most human and some animal plasmas to form a kind of thrombin (Smith and Hale, 1944). *Staph. pyogenes* is the name now given to all coagulase-producing staphylococci.

Staphylococcal exotoxins

Culture filtrates of *Staph. pyogenes* contain at least two haemolysins, the more important α-haemolysin which lyses both rabbit and sheep red cells at 37° C. and the β-haemolysin which fails to haemolyse rabbit cells, but destroys sheep cells in the cold (Glenny and Stevens, 1935). These two haemolysins produce two different antitoxins.

Staphylococcal toxin (culture filtrate) destroys white cells as well as red cells, and is on that account called a leucocidin. It will also produce a spreading necrosis of the skin if injected intradermally into a rabbit (dermotoxin) and will kill rabbits if injected intravenously. Kellaway, Burnet and Williams (1930) ascribed the lethal effect to a direct action on heart muscle. Intravenous injection of doses too small to kill produces cortical necrosis of the kidney (de Navasquez, 1936).

Opinion is divided as to whether these various toxic actions are due to one or to several different toxins. Probably the leucocidin, dermotoxin, lethal toxin and renal toxin are all associated with the α-haemolysin, if they are not the same thing. All five effects are neutralized by antitoxin made against α-haemolysin, or against toxoid prepared from it.

Diphtheroid bacilli other than true diphtheria bacilli are very common in wounds, especially in the later stages of their treatment. Most of these are easily distinguished from diphtheria bacilli by their morphological and cultural properties, but sometimes non-toxigenic diphtheroids very closely resembling diphtheria bacilli are present in wounds, and these can be distinguished only by means of a virulence test, which is therefore a necessary part of the bacteriological diagnosis of wound diphtheria. Small cuts and abrasions are also liable to infection with the diphtheria bacillus.

The "desert sore" familiar in the Middle East sometimes became infected with diphtheria bacilli, but it is most unlikely that diphtheria bacilli had anything to do with the general aetiology of "desert sores". *"Desert sores"*

(2) Gram-negative bacilli

Any of the Gram-negative bacilli which cause the acute specific fevers—the typhoid, paratyphoid and dysentery bacilli and the *Salmonella* group—may be found in abscesses, in infected urine or even in wounds. Under such circumstances they do not usually harm the patient much more than do the commoner but less "pathogenic" *Proteus, Pseudomonas pyocyanea* and coliform bacilli. *Proteus, Ps. pyocyanea*, or *Bacterium coli* may occasionally be isolated from the blood of a septicaemic patient.

Chemotherapy, which controls these organisms less easily than it does the pyogenic cocci, has emphasized their importance in wound infections. Because they are insensitive to penicillin, they are the chief bacterial risk of penicillin therapy, causing occasional abscesses round intramuscular drip needles, meningitis following intrathecal penicillin, or even septicaemia after the intravenous use of contaminated penicillin. *Complications of penicillin therapy*

(a) *Wound infections*

Gram-negative bacilli infect wounds both early and late. Fleming (1915) pointed out that the flora of most wounds changes from a non-specific initial pattern, which may often be faecal in type, to a later and more uniform one in which pyogenic cocci and diphtheroid bacilli predominate. Coliform bacilli, with Clostridia, aerobic spore-bearing bacilli, micrococci and various other non-pathogenic bacteria are commonly found in early wounds within a few hours of their infliction. In the later stages of treatment, wounds usually acquire added infections with pyogenic cocci, diphtheroid bacilli, coliform bacilli of various kinds, *Proteus* or *Ps. pyocyanea* (Miles, 1944).

Late infections of wounds may often be shown to come from reservoirs of infection in the neighbourhood. The chief reservoirs of the pyogenic cocci are upper respiratory passages; but Gram-negative bacilli, other than members of the genus *Haemophilus*, are not very often found in throats and noses; their chief reservoir in a ward consists of the other wounds therein (Miles and others, 1940). De Waal (1943) has shown that contamination with coliform bacilli is commoner in wounds of the thigh and abdomen than of the hand and arm, suggesting that faeces constitute another reservoir.

Ps. pyocyanea is a more obvious cross-infector of wounds than are other bacteria because it produces a blue-green colour on dressings. It is no more active in spreading round a ward than are other wound bacteria. It has acquired a reputation, probably equally undeserved, for displacing other bacteria, including pyogenic cocci, from wounds. The flora of a wound

the number of staphylococci in it. Wounds yielding cultures of staphylococci but showing no signs of clinical sepsis they call "silently infected". Such silent infections are chiefly important because they constitute a reservoir whence other wounds may be infected, not necessarily silently. Gissane, Miles and Williams (1944) have produced some evidence that "silent" infection may delay healing, though not so much as does frank clinical sepsis.

Virulence

Different strains of *Staph. pyogenes* vary in virulence. For instance, the Bundaberg strain, which caused a series of accidents following the injection of contaminated diphtheria prophylactic, was highly virulent as judged by its effects on the sufferers, and was also powerfully toxigenic. Measurement of virulence is difficult because rabbit tests cannot be directly related to man and there is no direct test that can be made on man. Kouritsky and Mercier (1940) find that most human nose strains are of low virulence for the rabbit. The same authors state that virulence for the rabbit can be modified by "passage".

Some strains have been identified as responsible for or associated with epidemics, usually of pemphigus neonatorum (Elliott, Gillespie and Holland, 1941; Hobbs, 1944).

Identification

As yet there is no simple method of labelling strains of staphylococci, comparable with Griffith's method of typing haemolytic streptococci. Cowan (1938, 1939) has differentiated three serological types to which most strains belong, but so small a number of types does not allow sure labelling among strains of so common an organism. A more promising technique is provided by the study of sensitivity of different strains to bacteriophages, of which a wide selection may be obtained from lysogenic staphylococcal cultures (Fisk, 1943; Wilson and Atkinson, 1945). Probably this new method will considerably enlarge knowledge of staphylococcal diseases.

5. OTHER BACTERIA OF SURGICAL INTEREST

(1) Diphtheria bacillus

Wounds

Diphtheria bacilli may infect wounds. They are particularly likely to do so in communities in which the carrier rate is high or faucial diphtheria is present. Bensted (1936) described a limited outbreak of cutaneous and faucial diphtheria in India which responded well to a policy of Schick testing and immunization.

The three varieties of diphtheria bacillus, *gravis*, *mitis* and *intermedius*, are much alike in their effect on wounds. Wound diphtheria does not usually make the patient very ill, although it should be nursed with the usual precautions for diphtheria. The most serious of its effects is diphtheritic paralysis. MacGibbon (1943) noted peripheral neuritis (paralysis) in 26·8 per cent of 71 cases of wound diphtheria; Cameron and Muir (1942) in 12 out of 66 cases. Paralysis may not develop until after the wound is healed.

Post-diphtheritic neuritis

A wound infected with diphtheria bacilli does not appear very different from other infected wounds. There may be a membranous slough on its surface, or the granulations may be covered by a thin, misty film, easily overlooked. The skin immediately around the wound may be anaesthetic. In the absence of paralysis, clinical diagnosis is often not made, and cases are easily missed unless bacteriologically examined.

Tetanus toxin probably acts like strychnine on synaptic junctions and mu end-plates of motor nerves, lowering their threshold and annulling recipro inhibition of antagonistic muscles, so that small stimuli cause exaggerated muscular responses and clonic contractions and spasms. The paralytic action of the toxin of *Cl. botulinum* is the reverse of that of *Cl. tetani*.

Cl. welchii toxin

The toxins of other pathogenic clostridia are less physiologically specific *Cl. welchii* produces seven toxins differing from one another in antigenic specificity and in action. Of these, only one—the α-toxin—is known to be of pathological importance to man, the virulence of *Cl. welchii* depending upon it. For a review of the subject of *Cl. welchii* toxins, *see* Oakley (1943) and Evans (1945).

In the presence of calcium ions, the α-toxin is haemolytic; it is also dermo necrotic. Injected intravenously, large doses kill in a few minutes, smaller doses causing a rise of blood-pressure, intravascular haemolysis, haemorrhages and a marked haemolytic anaemia, followed by death. The α-toxin is also a lecithinase which can liberate free fat from the lipoids of human serum or egg yolk (Seiffert, 1939; Nagler, 1939; MacFarlane, Oakley and Anderson, 1941; MacFarlane and Knight, 1941). It is therefore the first bacterial exotoxin for which a chemical action has been defined. Frazer and others (1945) have suggested a bearing which the action of α-toxin may have on the pathology of fat embolism, although they do not claim that *Cl. welchii* is an important cause of fat embolism.

α-toxin and embolism

The remaining 6 toxins of *Cl. welchii* are either haemolytic, lethal or necrotic. They are not lecithinases and are not important in human pathology.

Strains of *Cl. welchii* which produce predominantly the α-toxin are called Type A strains, and include strains known to be pathogenic to man, and also the great majority of strains from human faeces. Types B, C and D are mainly of animal origin. The virulence of human strains depends upon the α-toxin (Evans, 1945).

(*b*) *In the gut*

Practically every sample of human faeces contains toxigenic *Cl. welchii* of Type A (Borthwick and Gray, 1937; Taylor and Gordon, 1940). If toxin is produced in the gut, it is rapidly destroyed and does not enter the blood stream. Normal human sera have a very low antitoxin content. Clostridial toxins play no demonstrable part in the "toxaemia" of intestinal obstruction, but may do so in gangrenous appendicitis and intestinal perforation, since patients recovering from these two conditions possess abnormally high antitoxin titres (Bower and others, 1938).

Cl. tetani occurs in only about 5 per cent of human faeces samples, and may be an accidental contaminant rather than a normal faecal resident.

(*c*) *Surgical accidents*

On rare occasions, tetanus and gas gangrene have occurred after "clean" surgery. Possible sources of infection are catgut, which, however, can nowadays be sterilized so as to be safe, cotton-wool, especially of the brown variety, air and the patient's faeces.

Unless autoclaved, cotton-wool is usually impregnated with spores (Puerperal Tetanus Report, 1941). Felt or cotton-wool used to pad a plaster may produce tetanus if a plaster sore develops.

sometimes changes quite suddenly, the species originally present being replaced by others, but *Ps. pyocyanea* has no greater tendency to take part in such a change than have coliform bacilli or *Proteus*.

(*b*) *Burns*

Gram-negative infections of burns are important. Colebrook (1945) considers that they delay healing and produce fever. *Ps. pyocyanea* is one of the few bacteria to interfere seriously with the success of Thiersch grafts.

(*c*) *Urinary infections*

Gram-negative bacilli and staphylococci are the bacteria chiefly associated with urinary tract infections. Many different kinds of coliform bacillus are implicated. Burke-Gaffney (1933) reports that *Bact. aerogenes* is commoner in urines than are faecal types of *Bact. coli*. Dudgeon (1924) isolated from infected urines strains of "paracolon" bacilli which differed from the typical *Bact. coli* in that they fermented lactose late or not at all, and might be haemolytic on blood-agar plates. Sandiford (1935) has shown that similar "paracolon" bacilli are commonly found in faeces. They are not more harmful than other coliform bacilli, but patients with almost any kind of Gram-negative bacillus infecting the urinary tract may be ill enough to be suspected of enteric fever.

Dysentery bacilli (including *Bacterium alkalescens*) and *Ps. pyocyanea*, *Bacterium alkaligenes*, *Haemophilus influenzae* and other kinds of Gram-negative bacilli may infect urine. The flora of an infected urinary tract, like that of a wound, may change from time to time.

Special importance is attached by Cook and Sutton (1939) and by Chute and Suby (1940) to *Proteus* infections, because the great activity of this species in splitting urea may favour calculus formation, by making the urine alkaline and removing urea which helps to keep phosphates in solution. Most of the bacteria found in urine are thought to aid calculus formation (Lett, 1936).

(3) Clostridia (anaerobic spore-bearing bacilli)

(*a*) *General*

The anaerobic spore-bearing bacilli grow only in media with a low oxidation-reduction potential. They are called anaerobes because they will not grow in ordinary media in the presence of atmospheric oxygen, but the O–R potential of ordinary media can be lowered sufficiently for their growth even in the presence of atmospheric oxygen by adding to it suitable reducing agents such as lumps of boiled meat, sterile iron filings or iron wire, or even cotton wool. Machinery for excluding oxygen is needed only for making plate cultures.

In soil and in animal and vegetable waste, local areas of low O–R potential are probably produced by the chance chemistry of organic matter, and by the growth of aerobic micro-organisms. Clostridia are widely distributed in soil, especially if it is contaminated with faeces of man or animals. Of species pathogenic to man, all except *Clostridium botulinum* are frequent in the gut and in faeces.

Toxins

During growth, pathogenic clostridia secrete powerful, unstable exotoxins which are readily converted into toxoids suitable for the active immunization of man and animals. The use of tetanus toxoid, together with prophylactic tetanus antitoxin, has practically eliminated tetanus from war surgery.

World War II. His figures do not differ much from those of World War I, but earlier accounts of *Cl. oedematiens* need careful interpretation, for without animal tests, which are often difficult to perform under war conditions, other non-toxigenic clostridia such as *Cl. bifermentans* may be mistaken for *Cl. oedematiens* which they resemble.

Meleney (1935) quotes four fatal cases of post-operative infection due to *Cl. septicum* present in catgut.

6. SKIN

Surgeons are concerned with the bacteriology of the patient's skin at the site of operation, and of the skin of their own hands and those of nurses. A review of the subject of skin disinfection by Colebrook (1941) should be consulted.

Transient flora

The superficial flora of the skin is largely transient and is derived from the environment. The transient flora of fingers comes from handkerchiefs—a rich source of infection—and, at appropriate times of the day, from faeces. The fingers of nurses and surgeons pick up bacteria from dressings. It is easy to demonstrate the pathogenic bacteria on a dressing, which is not macroscopically stained with pus, by placing fragments of it on blood agar and flooding with melted agar. Discrete colonies form on the cotton fibres, and give a visual picture of the kind and degree of infection.

The transient flora of the skin is easily removed by washing or by rubbing with spirit or a detergent like Cetavlon. Swab tests on skin cleansed by washing indicate that the chief cleansing effect is mechanical. To rid one square inch of skin of its transient bacteria, a considerably larger area, say 4 to 8 square inches must be washed. In cleansing skin areas before giving injections, the size of area cleansed is more important than the kind of fluid used for the purpose. Very small areas cannot be cleansed at all. Spirit gives a better result than most of the ordinary fluids used, though others are satisfactory.

The bactericidal power of the skin, already referred to, helps to remove transient bacteria, and provides a good "rationale" for the practice of cleansing an operation site 24 hours before operation. Skin cannot be sterilized.

Resident flora

The resident flora of the skin is usually non-pathogenic, consisting of coagulase-negative staphylococci and diphtheroid bacilli. In about 5 per cent of cases, however, the resident flora of the hand include *Staph. pyogenes* (Devenish and Miles, 1939). Price (1938) has shown that the resident flora may change, and that those working in surgical wards are liable to acquire pathogenic bacteria which become resident.

No known cleansing method will remove the resident flora, which lie deep in the hair follicles and sebaceous glands (Lovell 1945) but probably not in the sweat glands or their ducts.

"Scrubbing up"

"Scrubbing up" does not materially affect the resident flora. This fact can easily be, and should be, demonstrated to nurses and students by a simple experiment. A sample from 1 square inch of skin from the back or palm of the hand is taken with a swab moistened in sterile broth. The hand is then "scrubbed up" for 5 or 10 minutes in hot running tap water (which is almost sterile) with nail-brush and soap, well rinsed, and dried on a sterile towel. A second sample is then taken from the same area with a broth-moistened swab, which is thoroughly rubbed over the area for 30 seconds. Usually the

The risk of infection from air is likely to be small, and no accidents proved to be due to infection with air-borne clostridia can be quoted. The risk might however, be significant if operating theatre air were heavily contaminated with dust from the street.

The patient's gut may provide infecting clostridia if it is perforated. Clostridial infections are said to be more frequent in pelvic than in other kinds of surgery.

Spores may remain alive in old wounds and scars for long periods. Bonney, Fox and MacLennan (1938) isolated *Cl. tetani* from the abdominal scar of a woman who ten years previously had suffered from tetanus following uterine myomectomy and had recovered. It has been suggested frequently that clostridial infections for which no other cause can be found may have been due to such spores long resident in the tissues. Normal tissues have an O–R potential too high to allow the germination of clostridial spores (Fildes, 1927, 1929). Death of tissue or secondary infection may lower the O–R potential enough to permit spores long resident in the tissues to germinate, but "idiopathic" clostridial infection which can be truly explained in this way must be very rare.

Injection accidents

Gas gangrene and tetanus have followed injections (Medical Research Council *War Memorandum* No. 15). Such accidents are probably usually due to contamination of the spirit in which the syringe is "sterilized".

(*d*) *Wound infections*

Most clostridial infections of wounds are harmless. *Cl. welchii* occurs in about a third of all early wounds (Altemeier and Gibbs, 1944; Spooner, 1941a), but under 1 per cent of wounds are complicated by gas gangrene or anaerobic cellulitis (MacLennan, 1944). From most wounds, *Cl. welchii* dies out. Occasionally it persists for months in a wound without doing any harm. Those strains which remain in wounds for long periods of time without doing any damage may nevertheless be toxigenic (Robertson and Keppie, 1941).

Clearly, the mere presence of clostridia in a wound is not enough to initiate either "anaerobic cellulitis" or "anaerobic myositis" (true gas gangrene). Pure bacteriology does little to answer the long-debated question of the pathology of these two conditions. The question seems to hinge on the difference between virulence as judged on toxin production and inoculation of experimental animals, and invasiveness, or the ability to gain a foothold in tissues and to spread in them. Arterial injuries and the presence of dead muscle in a wound seem to favour invasiveness, possibly by allowing clostridia to enter a phase of logarithmic growth.

Cl. tetani, like *Cl. welchii*, may be present in wounds without causing disease (Altemeier and Gibbs, 1944). As a complication of surgery, tetanus is no longer very important, but sporadic cases occur in the unimmunized.

Of other clostridia, the two most important to surgery are *Cl. septicum* (*Vibrion septique*) and *Cl. oedematiens*. Both produce strong exotoxins resembling in their general actions the toxins of *Cl. welchii*, but antigenically specific. Both are associated with gas gangrene and may be the only pathogenic clostridia implicated, although usually they occur in mixed infection with the far more important *Cl. welchii*. MacLennan (1943, 1944) reports a high incidence of *Cl. oedematiens* in infected wounds in North Africa in

Routine". Of these, routine is the most important, but the routine must be made in the light of bacteriological knowledge, or much time and soap and water will be wasted.

8. CHEMOTHERAPY

There is not space in an article of this kind to do more than mention chemotherapy. The subject has developed enormously in the past five years, and its ultimate effect on surgery cannot yet be predicted. It is already clear that the main rôle of chemotherapy is curative rather than preventive. Suitably selected cases of infection due to bacteria which are sensitive to the chemotherapeutic drugs used respond very well indeed to treatment either with sulphonamides or with penicillin. In war wounds, penicillin has indeed had a very impressive success as a preventive agent as well as in the cure of established infections.

Chemotherapy, however, does not at present provide protection against all bacteria. For instance, Gram-negative bacilli are insensitive to penicillin and nearly so to sulphonamides; and sulphonamide-resistant strains of *Str. pyogenes* possess all the pathogenic capacity of sensitive strains. The effect of wholesale prophylactic use of sulphonamides in a ward seems to be to convert the predominant bacterial species into resistant species.

Colebrook (1945) refers to several instances in which sulphonamide-resistant strains of *Str. pyogenes* have produced ward epidemics.

Although strains of *Staph. pyogenes* resistant to penicillin are found, and are not uncommon, all strains of *Str. pyogenes* seem to be sensitive. Under experimental conditions in the laboratory, resistant strains of bacteria normally sensitive may be produced, but what little evidence there is on the subject suggests that under natural conditions strains resistant to penicillin are less readily produced than are strains resistant to sulphonamides.

Gram-negative bacteria

Neither penicillin nor the sulphonamides are effective against Gram-negative bacteria. It is not too much to hope, however, that chemotherapeutic agents capable of controlling them will soon be found. Already at least two have been favourably reported on—Gramicidin S, described by the Russian workers Gause and Brazhnikova (1944), Belozersky and Passhina (1944) and Sergiev (1944); and the monophenyl ether of ethylene glycol, called Phenoxetol (Berry, 1944), but it is too early yet to pass a reliable judgment on either.

Chemotherapy has made the universal application of aseptic bacteriological techniques more necessary rather than less so, for the chemotherapeutic agents themselves have to be dispensed and administered with precautions against contamination by resistant bacteria.

While chemotherapy gives surgery great added safety and increased scope, the best kind of surgery will still depend upon the best possible kind of aseptic technique, and an understanding of bacterial disease must necessarily rest on knowledge about the bacteria producing it.

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second sample yields a growth of bacteria almost as great as the first. Thorough rubbing for 30 seconds brings the resident bacteria to the surface.

Rubber gloves A hand inside a rubber glove soon becomes heavily coated with bacteria which work their way up from the deeper structures of the skin as the hand is subjected to movement and pressure. Devenish and Miles (1939) published graphic evidence of the large quantities of such bacteria which may escape through a small glove puncture. Rubber gloves are very commonly punctured. Weed and Groves (1942) found that 22·6 per cent of the gloves used in 4,549 operations were punctured. Perforations in rubber gloves probably account for most of the minor sepsis traceable to the operating theatre, droplet infection from the throats of the theatre staff accounting for nearly all the rest.

7. SURGICAL TECHNIQUE

Operating theatre Apart from the accidents due to punctured rubber gloves and imperfect masking, it is probable that the risk of accidental infection in an operating theatre is very small indeed, provided that the usual full aseptic technique of the theatre is strictly observed.

It is difficult to assess the number of minor and major theatre infections that occur. Meleney (1940) gives the figure of 2·6 per cent of "clean" operations which become infected, mostly not seriously. Hirschfeld (1941) on reviewing the published records of various authors, eighteen American, one British and one French, concluded that the infection rate among "clean" cases is about 3 to 5 per cent.

If, as is desirable, the incidence of operative infections is to be reduced still further, bacteriology would indicate rubber gloves and infected or carrier throats as the two main subjects deserving attention. The hazard from infected theatre air is in any case small, and can be still further reduced by the use of special, clean, frequently sterilized theatre blankets, a patient's own blanket never coming into the theatre.

Ward technique In the wards, a different bacteriological technique is required. Wounds made in the theatre and closed by primary suture while still in the theatre *run little risk in the ward. Probably they are not uncovered and exposed to* infection until healing is far enough advanced to render the risk of infection negligible.

Open wounds that require dressing in the ward are, however, in a different class, for they are exposed to infection from dust, droplets and by contact. A technique for dressing wounds without introducing bacteria into them is suggested in the Medical Research Council *War Memorandum* No. 6. That application of the principles laid down in this memorandum will reduce the incidence of ward infection has been shown by McKissock, Wright and Miles (1941) and by Williams and others (1944).

The bacteriologist can contribute to the control of ward infection by formulating a picture of the bacteriology of the ward as one ecological picture, the bacteriology of any one patient being an incident in the main picture. Practical instruction of nurses in the simple exercises suggested above, and in swabbing their throats and fingers, aids their appreciation of the necessary drill. In 1899 Sir Cuthbert Wallace wrote: "The three most important factors in securing asepsis in surgery are Soap and Water, Time, and

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BASAL METABOLISM

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1. DEFINITION

49.] By basal metabolism is meant the lowest output of energy by the body. There are various forms of energy such as heat, light, sound, electricity, magnetism, potential or static energy, and mechanical energy or work. Of these forms of energy, the human body is most interested in heat, so we may change our definition by saying that the basal metabolism is "the lowest output of heat the body produces". Strictly speaking the conditions under which we measure the so-called basal metabolism or basal heat output do not give the lowest reading—for this occurs during sleep—but the term basal metabolism or basal metabolic rate (B.M.R.) has, despite this objection, retained its place in text-books. *Heat*

2. FACTORS AFFECTING BASAL METABOLISM IN HEALTH

Before giving details of the preparation of patients for this test, it is well to know the factors which influence the heat output of the body.

(*a*) *Food*

The ingestion of food causes an increase in the heat output of the body, due to the increased work of the digestive organs, and to the entry into the blood stream of food derivatives which are capable of stimulating cellular metabolism. This stimulating effect of food or, as it is called, its specific dynamic action lasts approximately 12 to 14 hours. Of the various foodstuffs protein has the *Protein* greatest and most prolonged specific dynamic action, a large intake increasing

the heat output for more than 14 hours afterwards. Water does not raise the basal metabolism appreciably unless it is taken in large amounts or unless it is iced.

(*b*) *Exercise*

Any form of mild exercise such as walking, climbing stairs, cycling and the like can be compensated for by resting on a couch for half-an-hour. Much confusion has arisen over, and mis-statements have been made about, the effect of exercise on the heat production. This problem has been investigated by Robertson (1944) when it was clearly shown that despite moderately severe exercise, by resting on a couch for 20 minutes the increase in heat output due to the exercise had completely disappeared. It is interesting to note that patients with thyrotoxicosis, like normal subjects, require a rest of only twenty minutes to reproduce basal conditions. These findings are of importance because it is still not sufficiently appreciated in Great Britain that a satisfactory and accurate reading of the basal metabolism can be obtained on "out-patients". The customary blocking of a hospital bed for several days for this examination adds considerably to its cost and to the patient's inconvenience.

Effect of rest

(*c*) *Anxiety*

Anxiety and so-called nervous tension can appreciably raise the body's heat production. Nervousness is not uncommon at the initial test, and so these readings are commonly higher and sometimes much higher than subsequent or true basal determinations. Thus in a series of 223 nurses aged 19, 156 (70 per cent) gave initial readings which were significantly higher than those on the second day; 48 (22 per cent) gave results 10 per cent or more higher, 21 (9 per cent) gave results 15 per cent or more higher, and as many as 11 (5 per cent) gave readings as elevated as 20 per cent higher. Usually the increased basal metabolism due to anxiety disappears by the second day of the test. It is clear therefore that no test should depend upon a single reading.

Effect on tests

(*d*) *Body temperature*

Fever raises heat production in a quantitative manner. Du Bois (1936) has shown that a rise of temperature of 1° C. will raise the heat production by 13 per cent (7·2 per cent for each degree Fahrenheit). In reporting on a subject's basal metabolism 7·2 per cent must be added for every degree of fever.

(*e*) *Room temperature*

The temperature of the room can affect the basal metabolism. The heat production can be increased 30 to 50 per cent by shivering (Loewy, 1890; Martin, 1930). On the other hand uncomfortable warmth with sweating produces only a small increase (Benedict, Benedict and Du Bois, 1924).

(*f*) *Menstruation*

Wakeham (1923) and Hafkesbring and Collett (1924) maintain that the heat production rises in the few days preceding menstruation, and falls below normal during menstruation.

(*g*) *Pregnancy*

During the last 3 months of pregnancy there is a slight increase in the heat production.

3. PREPARATION OF PATIENT FOR TEST

In view of the fact that certain factors can increase the basal metabolism, certain conditions must be observed if the heat production that is measured is the so-called basal reading and these are:

(i) The patient must have fasted for 12 to 14 hours, and the last meal should contain a minimum of protein. It is important to exclude the drinking of tea, or even water, on the morning of the test.

(ii) The patient must rest quietly on a couch for half an hour before a reading is taken. *Conditions of investigation*

(iii) The room should be comfortably warm with a temperature in the region of 20° C.

(iv) It is well to avoid taking a reading during the 4 or 5 days before menstruation.

(v) To compensate for anxiety, nervous tension and the like, it is suggested that a uniform technique should be adopted, and one found practical is as follows:

The patient attends on 2 successive mornings after the customary fast of at least 12 hours. After half an hour's rest on a couch 2 readings each of 10-minute duration are taken. The readings on the second day are usually lower than those on the first, but if they are not, the patient is asked to attend on a further morning. On the day with the lowest reading the duplicates are expected to agree within 5 per cent (or attendance on a further day is requested), and the lower of the 2 readings is reported as the basal metabolism. *Preliminary rest*

4. TECHNIQUE

Of the various methods, direct and indirect, for measuring the heat output of the body, the simplest and the most practical is by estimating the oxygen consumption using a so-called closed-circuit apparatus, examples of which are the Benedict portable (Benedict, 1918), the Krogh (1922) and the Benedict-Roth (1922). Fig. 3 shows the Benedict-Roth with recording spirometer, one of the most satisfactory of the closed-circuit models. In this form of apparatus the determination of the respiratory quotient is disregarded, and the oxygen consumption alone is measured and from that figure the heat output is assessed. Flutter valves are used to direct the flow of air. An accurately timed kymograph records the movements of the spirometer bell upon a drum covered with a paper chart ruled vertically into accurately determined 1-minute spaces. The principle of the Benedict-Roth apparatus lies in its spirometer bell having a diameter of 16·24 centimetres and an area of 207·3 square centimetres in cross section. Thus when the level of the spirometer falls 0·1 centimetre in an experiment it means that 20·73 cubic centimetres of oxygen have been consumed. At a respiratory quotient of 0·82 (which is assumed to be present in this experiment for reasons to be explained later) 1,000 cubic centimetres of oxygen produce 4·825 calories of heat—in other words 207·3 cubic centimetres of oxygen produce one calorie of heat. Therefore a fall in the spirometer level of 0·1 centimetre means not only an oxygen consumption of 20·73 cubic centimetres but a heat output of 0·1 calorie. The respiratory quotient of 0·82 is chosen as this is the one of theoretical basal conditions. *Rationale* *Basal R.Q.*

It has been stated that the fundamental objection to the closed-circuit method for measuring the basal metabolism is the necessary assumption of an R.Q. of 0·82. This objection is unreasonable. Reference to tables on the relationship between oxygen consumption and heat production shows that if the body is burning only carbohydrate (R.Q. 1·00) a litre of oxygen produces 5·047 calories of heat, and that if the body is burning only fat (R.Q. 0·71) a litre of oxygen produces 4·683 calories of heat, that is, there is a maximal difference between those two extremes of only 7 per cent. Protein combustion

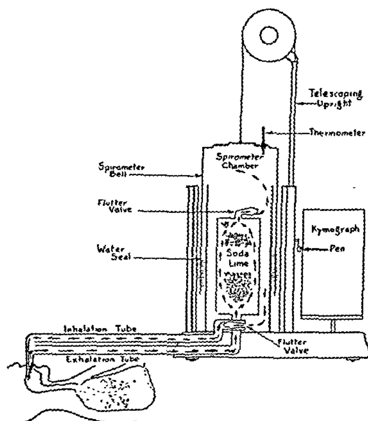


FIG. 3.—Benedict-Roth recording spirometer. (From *Basal Metabolism in Health and Disease*, by E. F. Du Bois.)

is not mentioned as, after a 12-hour fast the body mainly burns sugar and fat. If sugar and fat are being burned the R.Q. must lie between 1·00 and 0·71, and in practice it has been shown that by assuming an R.Q. of 0·82 the error is no greater and probably less than 1 per cent. This problem has also been studied by Robertson (1937) when a comparison was made between the open-circuit and closed-circuit methods for measuring the basal metabolism. It was shown that by assuming an R.Q. of 0·82 a correction rather than an error is introduced into the calculations, for the chances are that the measured R.Q. in a short-period experiment of 10 minutes is fallacious. This is due to the fact that the introduction of a mouth-piece or the application of a nose-clip or any face appliance alters the carbon dioxide output and thus vitiates the measured respiratory quotient.

Expression of basal metabolism as a figure

In expressing a subject's heat output as a percentage above or below normal, it is necessary to employ for comparison a set of normal standards. Several sets of normal standards are available and these include those of Aub and Du Bois (1917), Harris and Benedict (1919) and Dreyer (1920). It seems probable that the first set is the most satisfactory and the most universally employed. It depends upon the fact that the heat output in some way is related to the surface area or skin surface of the body. The surface area in square metres can be calculated from height and weight by the following formula:

Comparison with normal standards

Body surface area

$$\text{Weight in kilograms}^{0.425} \times \text{height in centimetres}^{0.725} \times 71{\cdot}84$$

Du Bois formula

but the calculation is made easier by reference to tables or charts computed from the above formula; for example a subject 59½ inches in height and weighing 87½ pounds has a surface area of 1·29 square metres. In addition a factor for age and sex has to be made, and this again is obtained from tables. Thus a normal woman aged 35 years has a heat output of 36·5 calories per square metre per hour; a man 39·5 calories. As one grows older so the heat output per hour per square metre of body surface falls; for example, a male at 14 years has a heat output per hour per square metre of 46 calories whereas at 70 years it has fallen to 35·5 calories.

5. NORMAL RANGE

The range of the normal basal metabolism is usually given as + 10 to − 10. This does not mean that an individual's heat output varies by twenty points, for indeed the basal metabolism varies as little from day to day as do the pulse and blood-pressure in normal healthy people. It is important when reporting on a basal metabolism to state the name of the normal standards employed. It is probable that the range of + 10 to − 10, using the standards of Aub and Du Bois, is too high for subjects in Great Britain. This means that results lower than − 10 are not necessarily of significance, and results above + 10 may be of significance.

6. EFFECTS OF DISEASE

In disease the basal metabolism may be raised above normal, it may be diminished, or it may be *within normal limits.* In the *first group* are included thyrotoxicosis, the leukaemias, polycythaemia vera, the active stage of hyperpituitarism, heart failure, fever and pregnancy. In the *second group* are hypothyroidism, hypopituitarism, malnutrition, nephritis with oedema, and Simmonds's disease (atrophy of the anterior lobe of the pituitary). The basal metabolism is essentially normal in any form of obesity unless associated with hypothyroidism, simple or endemic goitre, hypertension and hypotension, heart disease without failure unless due to thyrotoxicosis, nephritis without oedema, and in healthy people who are underweight or overweight.

Increase

Decrease

The diseases of metabolism of significant value in surgery—these alone will be discussed in detail—are thyrotoxicosis, heart failure and hypothyroidism.

(1) Thyrotoxicosis

This includes hyperthyroidism, toxic adenoma of the thyroid, exophthalmic goitre, Basedow's disease, Graves's disease and the like.

The basal metabolism is always raised in thyrotoxicosis; it may be markedly raised if the disease is severe or it may be only slightly raised if the disease is mild. In measuring the basal metabolism in such cases, excluding of course cases of heart failure, the same routine as that previously described is carried out. It must again be emphasized that it is unnecessary for thyrotoxic patients to occupy a hospital bed for this determination. Patients with thyrotoxicosis, like people with a normal metabolism, can easily compensate for moderate exercise such as walking or climbing stairs by simply resting on a couch for half an hour. Patients have travelled as far as 30 miles to the metabolism department and, after the customary rest, have given a satisfactory reading not significantly different from one taken at the bedside. The most important

Out-patient test

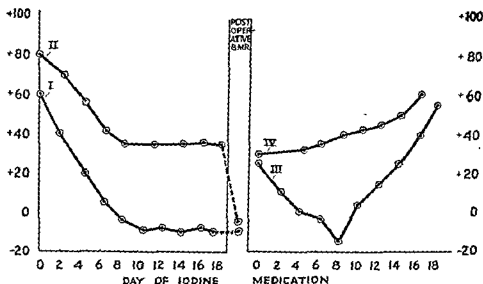


FIG. 4.—Four different types of reaction on basal metabolism to iodine administration in thyrotoxicosis.

factor which affects the heat output for a long period is not exercise but food.

Several drugs have the property of lowering the raised basal metabolism of thyrotoxicosis and these include iodine, iodides, thiouracil and its allied compounds.

(*a*) *Iodine*

It has been established that the minimal dosage of iodine that will produce the maximal clinical improvement and greatest fall in the basal metabolism is in the region of 6 milligrams of iodine or 1 drop of Lugol's solution. In practice, however, most surgeons prefer to give much larger doses in the region of 15 to 30 minims of Lugol's solution daily. It is customary in some clinics to give increasing doses of Lugol's solution of iodine beginning with 9 minims daily, rising to 30 minims before operation. No advantage is to be gained by this unnecessary complication in the dosage. It is easier from a nursing point of view, and as satisfactory therapeutically, to continue with constant large doses of 200 milligrams of iodine daily (30 minims of Lugol's solution) throughout the pre-operative period.

Effective dosage

Iodine appears to cause four clearly defined actions on the basal metabolism of cases of thyrotoxicosis and these are shown diagrammatically in Fig. 4. In the first, iodine causes the basal metabolism to fall to the patient's normal

level which means that the basal rate after iodine medication is the same as that after subtotal thyroidectomy. In the second, iodine can only partially control the thyrotoxicosis, and there is a further fall in the basal rate after operation. In the third, iodine causes a sharp fall and as sharp a rise in the basal metabolism. In the fourth, iodine makes the patient worse, and it causes the basal metabolism to rise. Subtotal thyroidectomy should never be carried out when the basal metabolism is rising as, for example, in reactions III and IV of Fig. 4, for this means that iodine has lost its power to control the toxicity, and surgery may precipitate a thyroid crisis. The ideal pre-operative condition of a case of thyrotoxicosis is one in which the basal metabolism is reduced to as low a level as possible, and is at the same time constant. The second condition is easier to obtain than the first; in other words curve II is

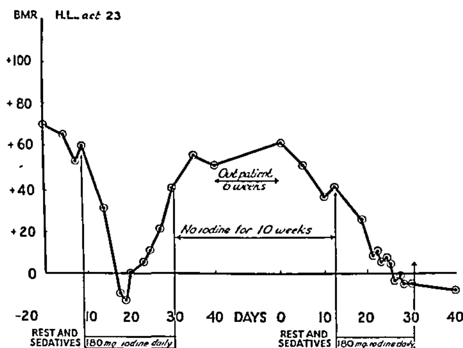


FIG. 5.—Chart showing B.M.R. curve in a case of so-called refractoriness to iodine.

commoner than curve I, with the result that many operations are performed on subjects with a high metabolism. One disadvantage is that the higher the pre-operative basal rate the more marked will be the post-operative reaction.

Interpretation of effects

In interpreting observations on the effect of iodine on the basal metabolism it is important not to rely on isolated readings, particularly in cases in which the basal rate rapidly falls and rises on iodine. In Fig. 5 the chart of such a case is reproduced. On iodine the basal metabolism fell rapidly from + 50 to — 13 in 10 days, but on the eleventh day it had risen to 0, on the fourteenth day to + 8 until on the twenty-first day of iodine therapy the basal rate had almost reached its initial and untreated level. In this case a reading on the fourteenth day of iodine therapy would have given the impression that the basal rate was falling, whereas in fact by the eleventh day iodine had lost its power of controlling the thyrotoxicosis and the basal metabolism had begun to rise. This

"Refractoriness"

condition of so-called refractoriness to iodine has been well described by Thompson and Thompson (1931).

It is the custom in most clinics to continue with iodine medication for several weeks or months after subtotal thyroidectomy, probably for two reasons. First, it is believed that iodine in some measure controls the toxic reaction following operations on toxic goitres and secondly, that it prevents regrowth of thyroid tissue and a recurrence or persistence of the thyrotoxicosis. These views have been investigated by Robertson (1946) and neither was found to be accurate. It was shown that iodine has no therapeutic value after operations on the thyroid gland if iodine has been given in adequate amounts before operation. It was further shown that post-operative iodine may have disadvantages, in that it may mask an active thyrotoxicosis which will become apparent only after the iodine is stopped, or when the patient becomes refractory to it.

Post-operative effects

It is well to remember that the basal metabolism is always raised in thyrotoxicosis. In mild cases the basal metabolism may be only slightly raised above, or even within, the limits of normal people. This fact has led to a misinterpretation of the basal metabolism findings. Thus the normal range of the basal rate is usually given as + 10 to − 10, so that a patient's initial basal metabolism of + 6 may be considered normal, as it lies within the normal range, but if the patient's normal basal metabolism were − 10, then + 6 would mean for him a raised basal metabolism. In such mild cases of thyrotoxicosis it is important not to rely on an initial metabolism, but to remeasure it after ten days on iodine. By using the basal metabolism in conjunction with iodine one of the most sensitive means of detecting thyrotoxicosis is obtained. Iodine has no effect on the basal metabolism of a normal person.

(*b*) *Thiouracil and thiourea*

Mode of action

Thiouracil and thiourea are believed to act by inhibiting the formation of thyroxine at its source in the thyroid gland. Both reduce the raised metabolism of thyrotoxicosis to normal or even to a myxoedematous level. These drugs cannot neutralize the effects of thyroid by mouth or thyroxine intravenously.

(2) Heart failure

In the absence of thyrotoxicosis the basal metabolism is increased only if dyspnoea is present and is due to overwork of the respiratory muscles.

(3) Hypothyroidism

The basal metabolism is diminished in hypothyroidism which includes myxoedema and cretinism. Myxoedema may be spontaneous or it may occur post-operatively after too radical a thyroidectomy. In either case the basal metabolism is markedly diminished. It is customary in some clinics to administer thyroid in doses up to 1 grain daily in order to counteract a degree of hypothyroidism which, frequently, is present in the 6 months following subtotal thyroidectomy for the relief of thyrotoxicosis.

Prophylaxis

7. SUMMARY

The basal metabolism is always raised in active thyrotoxicosis. The action of iodine on the raised basal rate of thyrotoxicosis can be summarized briefly:

(i) Iodine and all its compounds are equally effective. Roughly 30 minims of Lugol's solution has the same action as 4½ grains of potassium iodide. Each contains approximately 200 milligrams of iodine.

(ii) The maximal beneficial effect of iodine may be reached in as few as 6 days or as many as 25 days. Iodine appears to have four well-defined actions in thyrotoxicosis—two favourable and two unfavourable to operative procedures.

(iii) Isolated readings of the basal metabolism after iodine medication has begun may be misleading. Thus the impression may be gained that the basal metabolism is falling, whereas it is beginning to rise after a preliminary fall because iodine has failed to control the thyrotoxicosis.

(iv) There is no advantage in giving iodine after subtotal thyroidectomy for thyrotoxicosis.

(v) The basal metabolism is raised in heart failure without thyrotoxicosis, only if dyspnoea is present.

(vi) The basal metabolism is diminished in hypothyroidism, which is frequently seen in the six months following operation for the relief of thyrotoxicosis.

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[References to other titles are given under Basal Metabolism in the Index Volume. The subject of Basal Metabolism is also dealt with under the heading of Metabolism, Basal, in the *British Encyclopaedia of Medical Practice* (1938), Vol. 8, p. 588.]

BEDS, PLASTER

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1. INDICATIONS

50.] Plaster beds are designed to provide good immobilization of the trunk, and, by prolongation to include the head and limbs, to extend this immobilization to these parts.

The common indications for their use are as follows.

Tuberculosis

(i) Tuberculous disease of the spine or sacro-iliac joints.

Bony injuries

(ii) Certain fractures and fracture-dislocations of the spine, including those complicated by paraplegia.

(iii) Anterior poliomyelitis and certain other paralyses involving the trunk or abdomen, or the muscles of the pectoral and pelvic girdles.

(iv) Other chronic lesions of the bones and joints of the spine, for example, Calvé's disease, Scheuermann's disease, spondylitis rhizomelica, osteomyelitis of the spine and prolapse of the intervertebral disc.

(v) For fixation of the spine and sacro-iliac joints, following operative intervention, usually with a view to fusion.

Posterior shell

The *posterior shell* or bed is constructed to fit the patient, lying in the desired position, as regards both the trunk and the limbs.

This posterior shell is furnished with an *anterior shell* or *turning-case*, made to fit the patient lying in the plaster bed. When both are applied to the patient and are strapped together, he can be turned on to his face without any movement being possible. Removal of the posterior shell exposes the back, for treatment to the skin. While remaining on his face in the anterior shell, the patient is given relief of weight-bearing to his back, and enjoys a pleasing change in his orientation.

Finally, an anterior bed may be constructed to act as the main immobilizing agent. Under this routine the patient will be expected to develop his erector spinae muscles in elevating his head, and often shoulders as well, from the

bed. The immobilization is much less complete but allows movement only into hyperextension. Compensatory lordoses will form and the patient will develop the essential muscles for the protection of the spine, when the plaster shell gives way to the much less effective immobilization of a back brace.

Compensatory lordosis

This anterior shell routine is therefore applicable only to the later stages of treatment.

2. TYPES

The following types of bed are in use.

(i) Long posterior bed, including the head (Fig. 6).

(ii) Long posterior bed (Fig. 7).

(iii) Short posterior bed (Figs. 8 and 9).

(iv) Turning-cases to match each of the above (Figs. 10 and 11).

(v) Anterior shell for continued lying in the prone position (Fig. 12).

The long posterior bed will include the feet, while the short posterior bed extends only to the lower part of the thighs.

When the head is not included, the plaster stops at the root of the neck, not sufficiently far up to provide any prominent edge.



Fig. 6.—Long posterior plaster bed with head-piece. Note normal spinal curves and position of legs.

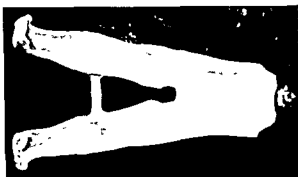


Fig. 7.—Long posterior plaster bed showing feet between right-angle position and 5 degrees of equinus. Note strengthening strut between knees.



Fig. 8.—Short posterior bed viewed from above showing narrow nursing aperture. This is to support the buttocks.

3. CONSTRUCTION

(1) Requisites

The following list of articles is necessary.

(i) A firm table somewhat longer than the patient.

(ii) Two firm pillows and 3 pairs of sand-bags of varying sizes, employed in positioning the patient.

(iii) Rubber sheeting to protect exposed portions of the table and pillows from plaster.

(iv) Plaster muslin (32 threads to the inch) of length and breadth 12 inches in excess of the bed to be constructed; 10 to 12 double sheets are needed.

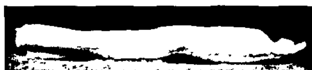


FIG. 9.—Short posterior bed (unmounted); lateral view.

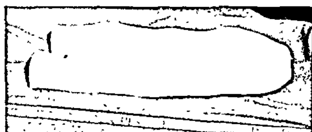


FIG. 10.—Turning-case, carefully moulded to iliac crests, costal margin and chest.

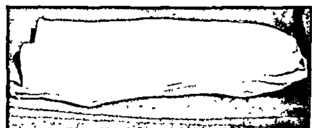


FIG. 11.—Turning-case under construction. May be modified to an anterior shell by a "cut-away" for nursing purposes and mounting on a frame or block.

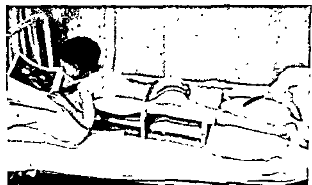


FIG. 12.—Short anterior plaster bed showing child raising head and shoulders and exercising erector spinae muscles; immobilization very incomplete; dorsi-lumbar kyphosis; pillow under shins to maintain knees slightly flexed and to avoid any hyperextension.

(v) Ten pounds of plaster (Terrey's Superfine Italian).

(vi) Twelve pints of water at 105° to 115° F.

(vii) Vaseline, strips of gauze and a bathing cap (Fitzgerald and Nissen, 1937).

(2) Positioning of patient

This all-important process is carried out by using the pillows and sand-bags. For a long posterior shell (Fig. 13A) the patient lies prone on one pillow, thus enabling the hips to flex 5 to 10 degrees over the lower edge of the pillow. The hips are abducted 10 to 15 degrees. The knees are flexed (5 to 10 degrees) by placing a sand-bag in front of each ankle, the feet projecting over the end of the table sufficiently to allow them to be at right angles to the shin. The feet are allowed neither to invert nor evert, and they should not point out more than 5 degrees, as it is undesirable to immobilize the hips in external rotation.

When the head is to be included, it will project beyond the upper end of the pillow and, the forehead resting upon something soft, the head will adopt a natural position with the neck retaining its normal moderate hyperextension.

Relaxation of paralysed muscles

When the upper arms are extensively paralysed, they will be placed at right angles to the trunk with the elbows bent to the required extent over the side

of the table. The position in these cases of paralysis is controlled by the need to relax those muscles most involved.

Turning-case

Positioning for the turning-case requires simply that the patient be lying in his posterior shell (Fig. 14A). This entails a delay in making the turning-case until the posterior shell is dry enough and strong enough to be so employed.

For an anterior bed, some hyperextension of the spine is sometimes desirable, whilst the lower limbs are in the restful position described above.



FIG. 13A.—Positioning in construction of long posterior bed. Note pillow; sand-bags under ankles and forehead; bathing cap and cotton-wool over ears.

Further preparation of the patient.—(See Fig. 13A.) The head is covered with a closely fitting bathing-cap or a cap made from a triangular bandage, pads being applied over the ears to make the head-piece more roomy over them. The face, when exposed, is covered by gauze; this is only to protect it from the drops of plaster, no anterior shell ever encroaching on to the face.



FIG. 13B.—Team about to apply first shaped plaster sheet. Note cotton-wool over hairy anal and axillary regions. Exposed skin covered with Vaseline.

Hairy parts

The whole of the body and limbs to be covered by the plaster shell is generously smeared with Vaseline to prevent the bed from sticking to the patient. For a similar purpose, hairy parts are covered in addition with a gauze pad.



FIG. 13C.—Later stages showing application of "cut-away" pieces over buttocks to strengthen this weak point; one assistant at left foot, one assistant rubbing body-piece.

(3) Team arrangement (see Fig. 13B and C.)

A team of three will manage a short posterior bed with ease.

Assistants' tasks

Five or six are needed for a full-length bed to include the head. One assistant attends to the plaster cream and supplies the gauze sheets duly saturated with cream; one stands by the side of each leg, for which limb he is responsible; one stands on each side of the trunk and together these two are responsible for hips, trunk and neck, while the sixth is occupied in making the head-piece.

(4) Making the plaster bed

The plaster cream is made by adding the plaster to the warm water, stirring vigorously the while. The muslin is passed through the cream and drawn quickly through one hand to remove any excess; the sheet, whether shaped or otherwise (Figs. 14B, 15, and 16), should drip freely but the plaster should not run off it.

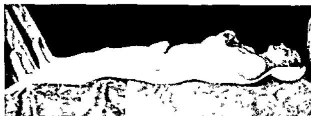


FIG. 14A.—Turning-case for long posterior bed with head-piece. Patient in trimmed and dried posterior bed; skin Vaselined; hairy regions covered.

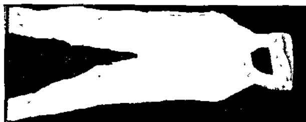


FIG. 14B.—Shaped plaster muslin (double layer) for turning-case for long posterior bed with head-piece.



FIG. 14C.—First shaped sheet applied to patient. (Face should be covered with gauze to avoid plaster splash.)

The sheet is spread out above the prostrate patient by the team ranged round the table, and is lowered on to the patient (Fig. 13B and C). By careful folding over the head and a generally lax application of the sheet, followed by rubbing, the plaster sheet is induced accurately to follow every contour of the patient. The plaster must not be allowed to encircle the trunk or legs beyond the mid-point in the sagittal plane—to do so may prohibit the removal of the plaster bed from the patient!—and these portions have in any event to be cut away.

Fitting to contour

The subsequent sheets are applied similarly, every assistant diligently rubbing the sheets together throughout the application. This rubbing is very important as it milks out air bubbles, and allows the whole to set as one mould, rather than in several layers; without it there is considerable loss in structural strength.

Air bubbles

Any bubble found later in trimming the plaster is a criticism of the person responsible for that portion of the bed.

The shaped legs in the full-length bed are connected by a plaster strut between the knees (Fig. 7) and the hip region is strengthened (Fig. 13C), in each case using the "cut-aways" from the shaping. In the case of an adult, alternate sheets are turned back along the sides to thicken the edge and give additional strength. All such adjustments are applied before the last sheet, which gives a final smooth surface.

The whole process of applying the plaster sheets should be accomplished

within 5 to 10 minutes, so that setting occurs with every sheet in position, and after adequate rubbing has ensured the closest contact between sheets and the absence of air bubbles.

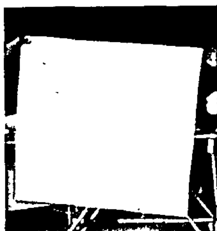


Fig. 15.—Oblong sheets of plaster muslin for short beds and turning-cases (double layers of muslin).

(*a*) *Trimming*

The plaster is now lifted off the patient, and turned over. The edges are trimmed before the plaster becomes too hard. A plaster bed should enclose rather more than half the depth of the patient, and a turning-case rather less than half. The cut-out for nursing purposes should be narrow so that the buttocks do not sink through the hole and become oedematous (Figs. 7 and 8). Free shoulder movement should be permitted by cutting the sides well away for the upper 6 inches of the trunk-piece. *Oedema*

(*b*) *Drying and finishing*

Drying should be accomplished in a warm dry atmosphere. Sufficient drying to allow of use is effected in about two days but complete drying takes over a week. The thickness of this plaster would be about $\frac{5}{8}$ inch, except where purposely thickened. This method of making a plaster bed combines maximal strength with least weight and the neatest finish; it appears to have originated in the clinic of Calot at Berck-sur-Mer. A well-made bed, adequately dried before being taken into use, should last for 12 months.



Fig. 16.—Shaped plaster muslin for long posterior bed; "cut-away" pieces preserved for strengthening weak points in plaster bed.

Occasionally it is desirable to waterproof the plaster bed. To provide a waterproof surface and at the same time to increase the strength and lasting properties of the bed, it may be treated with three coats of cellulose acetate paint (Bennett, Cohen and Kendall, 1937); between each coat an interval of *Waterproo*

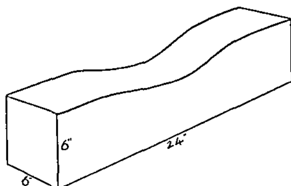


Fig. 17.—Wooden block. Two or three are required to support plaster bed.



FIG. 18A.—Short posterior plaster bed mounted on wooden frame; end-pieces of frame cut to fit curves of bed; wood screws pass through bed into end-pieces.



FIG. 18B.—Short posterior plaster bed showing webbing restrainers for children, apparent equinus, wooden frame and absence of lining

10 minutes is allowed for thorough drying. The cellulose acetate mixture is made by filling a 2-quart jar with cellulose acetate flakes (lacquer viscosity 5), adding 2 ounces of trimethyl phthalate A or "sizing" and then filling the jar with acetone. The jar is sealed and set aside for 3 to 4 hours, being stirred occasionally. The mixture will be about the thickness of paint but will thicken by evaporation of the acetone, if kept unsealed.

(*c*) *Supports*

Plaster beds for adults are usually supported on wooden blocks (Fig. 17). Two or three of these placed transversely on the mattress, over fracture boards, will give good support and allow clearance for nursing purposes.

Plaster beds for children are often supported on wooden frames, with end-pieces cut accurately to the curves of the bed (Figs. 18A and B). These



FIG. 19A.—Turning patient in plaster bed. Full length with head-piece.



FIG. 19B.—Turning-case applied and strapped.

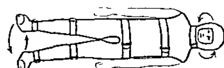


FIG. 19C.—Turning about a longitudinal axis.

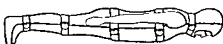


FIG. 19D.—Turned.



FIG. 19E.—Lying in turning-case with back exposed.

end-pieces are then engaged by countersunk wood screws passing through the plaster into the wood. This makes a very firm structure but, as the frame has to be lifted with the bed and turning-case when the patient is turned, it is not a satisfactory plan for the heavier adult case. Figs. 20A, B and C.

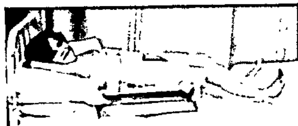


Fig. 20A.—Turning small child in short plaster bed using firm pillow. Note dorsiflexion to right angles, strap retainers, full exposure save for sun drawers.

Frames may be made unattached to the plaster bed, carrying the patient at an angle of 15 to 20 degrees; these provide an agreeable improvement in the range of vision without being open to any serious criticism where adult patients are concerned.



Fig. 20B.—Firm pillow in position. Two binders pinned under some tension; pins on side accessible after turning.

The 15-degree tilt can alternatively be provided by tilting the bed, but a flat mattress has distinct advantages.



Fig. 20C.—Child turned with plaster bed and attached frame and lying on pillow. Binders still in position. Equinus, showing full range is possible.

4. MANAGEMENT OF PATIENT

(1) Physical

Lining

A thin lining is usually employed in a plaster bed. It consists of a shaped piece of thin blanket stitched at the edge to a piece of cotton sheeting identical in size. Tapes may be used to hold it in place. A plaster bed without a lining is very comfortable but a washable lining has hygienic advantages. Young children are frequently nursed without a lining in their plaster beds as they are more likely to be restless and tend to get the lining wrinkled (Figs. 12 and 18B).



Fig. 20D.—Trunk well supported on firm pillow; two binders; fracture boards under mattress.

The patient needs turning at as long intervals as are compatible with

Pressure points

maintaining the pressure points comfortable and healthy. Inspection of the back is necessary almost daily for the first week in a plaster bed, with subsequent intervals of increasing length if progress is normal.

When sensation is normal, turning of an adult can be reduced to once in 4 to 6 weeks, in temperate climates, as soon as the patient and his skin have become accustomed to the bed.

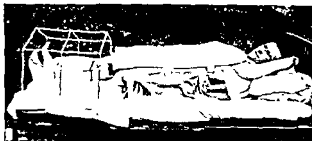


FIG. 21.—Turning-case strapped to short posterior plaster shell, ready for turning. Strap buckles on side accessible after turning.

Pressure sores

Anaesthesia of the back or limbs demands a much more cautious programme, pressure sores over the sacrum or heels being avoided only by the most vigilant and conscientious nursing.

Young children have to be turned over every 2 or 3 weeks as they are more liable to get crumbs and other particles inside the bed. These young children have to be watched as they may get larger objects inside their beds and fail to disclose the fact for fear of a reprimand.

The turning of an adult patient (Figs. 19 and 21) enclosed between his plaster bed and turning-case requires three strong men if it is to be done in an orderly manner, and without giving the patient the impression that he is in imminent danger. It is important to see that the strap buckles are on the side of the plasters, so that they may be accessible after turning.

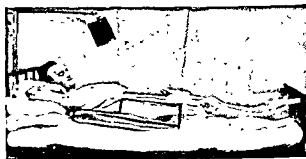


FIG. 22.—Adjustable mirror; bed-table to keep bed-clothes off feet. (Bed made of Perspex on metal frame.)

Children are sometimes turned without employing a turning-case, a pillow being strapped to the front of the child (Fig. 20). Immobilization is not so effective with this method, which, however, often suffices.

Treatment of the back

The exposed back should be washed with soap and water; some soap is then rubbed in and is followed by a mixture of equal parts of olive oil and spirit, dusting powder completing the treatment.

To remain in the turning-case for some hours is often appreciated as a pleasant change in a restricted existence.

Position of feet

The feet must not be allowed to sustain the pressure of the bed-clothes as this will result in equinus deformity (Fig. 21). A bed-table is frequently misused for this purpose (Fig. 22). In a short bed, the feet are allowed full movement and put through their range daily (Fig. 20A). The heels must be watched for signs of pressure, particularly in the paraplegic and the debilitated.

Position of knees

Knees must not be allowed to rest in full extension but always in some 5 to 10 degrees of flexion to avoid stretching ligaments (Figs. 12 and 14A).

Elbow rests are well illustrated in Fig. 24. Simple in construction, they are most helpful in supporting the upper arm and elbow.

Restraint of children

Small children often require restraining to prevent their sitting up in their plaster beds. The small bodice illustrated in Fig. 23 is one device. It may be put on over the upper part of the bed, being fastened behind and the tapes tied to the bedstead. Webbing straps may be used, as in Fig. 18B, or a wooden cross-piece may be added to the frame; this should cross the child's chest.



Fig. 23.—Bodice restrainer for small child for fastening behind and with tapes for tying to cot.

No clothes, save a pair of sun-drawers, are worn by the tuberculous patient when exposing himself to the invigorating fresh air and the controlled doses of sun. It is not possible for the most fastidious to wear more than a split nightgown, or a pyjama jacket worn back to front.

(2) Psychological

Environment

A leisurely atmosphere is advisable for these protracted cases; country surroundings and the company of other similar cases are much better than the city hospital with its disturbing turnover of short-term cases.

Entertainment

Occupation must be tackled methodically and with enthusiasm. A hospital school is the natural solution for children. For adults the need is both intellectual—reading, radio and television provide opportunities in this line—and physical, where rug-making (Fig. 24) and other forms of diversional occupation are so useful. Most forms of entertainment are a boon. Many cases can be transferred to a concert hall in the hospital premises if trolleys, with pneumatic wheels, and smooth pathways are provided. A concert hall, however, cannot take a large number of cases as they can only occupy the front of the hall, one row on the floor and one on beds or trolleys.



Fig. 24.—Diversional occupation—rug-making. Note padded arm rest and foot cage to allow exercises and avoid equinus.

The patient must be helped and encouraged to occupy the waking hours, even to use "each unforgiving minute". During World War II these patients have frequently been able to fulfil a further natural desire, and become almost self-supporting in performing jobs passed over to them from factories. Such a

Handwork

job is the wiring of parts of panels for aircraft, light delicate handwork, ideally suited for these handicapped people. When many such patients are collected together, occupation and entertainment are much more likely to be tackled with the energy demanded.

Various gadgets have been employed to help these patients. The tilted position has already been referred to. Prismatic spectacles give horizontal vision to those lying down. They take a little time to get accustomed to, and are not always the success which might be expected. An adjustable mirror is a great help particularly to cervical cases, where head movements are forbidden (Fig. 22).

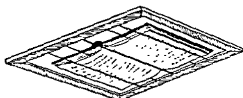


FIG. 25.—Overhead book support. Figure shows inner three wires supporting book; outer two elastic supports for loose surface pages.



FIG. 26.—Figure shows book lying on glass sheet; this must be removed for turning pages.

Reading

The book frames illustrated are usually much appreciated. (*See* Figs. 25 and 26.) When the book is supported by cross strings in the axis of the pages, these can be turned over from below. With a white ceiling, a projected image of a book can be read comfortably and mechanical page-turning can be provided.

The psychological management of these sorely tried patients demands attention and pays handsome dividends; inventiveness, enthusiasm and energy can combine to convert this period of incarceration into a more than tolerable chapter in a patient's life.

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[References to other titles are given under Beds, Plaster, in the Index Volume.]

BEDSORES

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1. DEFINITION

51.] Bedsore is the popular name for a lesion of cutaneous and subcutaneous tissues, which occurs in bed-ridden persons as the result of pressure.

2. AETIOLOGY

Bedsores are particularly liable to develop in persons suffering from prolonged debilitating illnesses, cachexia due to malnutrition, old age, general shock following injury or burns, and following lesions of the nervous system—in particular, spinal cord injuries.

3. MECHANISM

The factors determining the formation of bedsores can be classified as intrinsic and extrinsic. The most important intrinsic factor is the lowering of tissue vitality and tissue resistance to pressure, as the result of circulatory disturbances in the peripheral vascular system. The loss of vasomotor control, caused by paralysis of the nervous pathways subserving it, is very conspicuous in the early stages of spinal injury. Sensory loss in spinal lesions also plays an essential part, as afferent impulses from a pressed area, which normally elicit discomfort and thus incite change of posture, are abolished.

Intrinsic factors

Vasomotor control

Sensory function

Of the two extrinsic factors, pressure and maceration, the first is of cardinal importance. The degree and extent of the disastrous effects of local pressure are determined by its intensity, duration and direction.

Pressure

4. PLASTER AND SPLINT SORES

The present vogue of using plaster of Paris and splints in the treatment of fractured limbs and spine, and for flexion contracture of the legs in spinal lesions, has resulted in an increasing number of sores. The following factors are responsible for the formation of these sores.

(i) Careless moulding of the plaster and using plaster slab which is not sloppy but has already begun to harden.

(ii) Inadequate protection of bony prominences. This is especially disastrous in lesions of peripheral nerves and of the spinal cord.

(iii) Movement of a joint during the application of plaster, causing ridge formation and preventing smooth adaptation of the plaster to the contour of the limb. This occurs especially in patients with paraplegia of spastic type, accompanied by marked reflex spasms.

(iv) Allowing the plaster to take the weight of the patient's limb or trunk before it has completely hardened, thus producing flattening of the plaster, especially over the bony prominences.

(v) Friction at the edges of cock-up plaster splints for paralysed feet, and at the edges of bivalved walking plasters.

(vi) Pressure or friction by the iron and leather bands of calipers.

(vii) In cases of cauda equina and spinal-cord lesions, if the thigh band of the caliper is too long, its upper edge will cause pressure in the region of the ischial tuberosity.

5. BACTERIOLOGY

Bedsores always become infected, and the infection may become generalized. In spinal-cord lesions, this is often misinterpreted as due to ascending urinary infection. The micro-organisms most commonly found are: *Streptococcus haemolyticus*, staphylococci, *B. proteus*, *Bacillus coli*, *Streptococcus faecalis*, *Pseudomonas pyocyanea* and diphtheroids.

6. CLINICAL PICTURE

Sites

Sores commonly develop in areas over the skeletal prominences, especially the heels, malleoli, ischial tuberosities, trochanters and sacrum.

Various stages can be distinguished in the development of a sore.

Stage of transient circulatory disturbance.—Pressure has been sufficient merely to cause reddening of the skin, without destruction of the tissues. It promptly disappears if the pressure is relieved, and with massage.

Stage of permanent superficial circulatory and tissue damage.—Various types of sore result from this damage.

One is characterized by reddening and congestion of the pressed area, which does not disappear after decompression, and which leads to induration of the tissues.

Excoriation

In another type, the superficial layers of the skin have been killed and may be excoriated, exposing the weeping corium. In some cases in which the dead epithelium remains intact, it is raised by exudation from the living cells of the cutis beneath, and a blister develops. In other cases, damage extends to deeper layers of the skin and may lead to superficial necrosis and formation of an ulcer, often with a pigmented border.

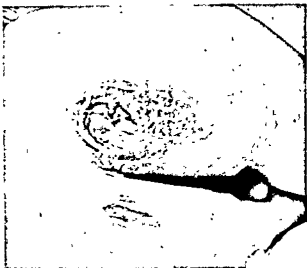
Superficial ulcer

Gangrene Deep ulcer

Stage of penetrating necrosis (*malignant sore*).—The destruction also involves the subcutaneous tissues, including fasciae, muscles and bones. It leads to gangrene and later to a deep ulcer. Often the necrosis of the deeper tissues is more extensive than that of the skin, which accounts for the undermining character of the sore (Figs. 27 (*a*)–(*c*) and 28 (*a*)–(*d*)) and the formation of deep sinuses.

7. TREATMENT

(1) Prophylactic



(a)

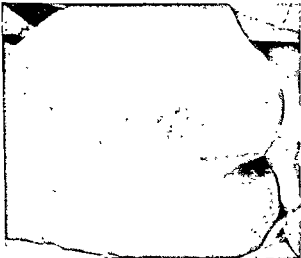
First aid

This is a vital procedure, especially after spinal injuries, when sores may occur within even a few hours after injury. First-aid precautions are: removing hard objects from the patient's pockets, padding bony prominences, counteracting traumatic shock, immediate transportation, preferably by



(b)

FIG. 27.—Malignant sore on right buttock. (*a*).—Penetrating necrosis involving fascial and deeper tissue. Note also superficial sore on left buttock. (*b*).—After excision of slough. (*c*).—Six months after complete healing.



(c)

air, to a Spinal Centre or a hospital dealing with spinal injuries.

Posture

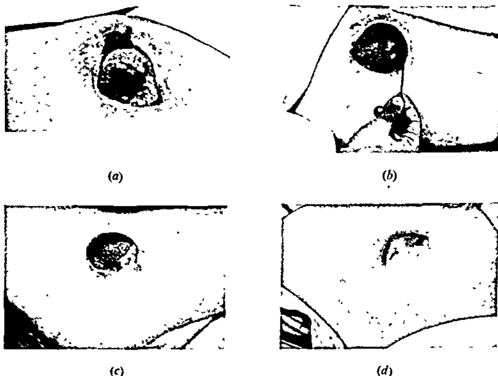
The cardinal method in local prophylaxis of pressure sores is change of posture. This must be carried out from the first—including the period of transit. As a rule, turning the patient at two-hourly intervals will be sufficient, but this must be carried out relentlessly day *and* night, despite reluctance to

Redistribution of pressure

disturb the patient's rest. Besides change of posture, redistribution of pressure by nursing the patient on a rigid bed equipped with a water, air or Sorbo mattress is of the utmost importance. Plenty of small pillows are also needed to support the limbs and trunk in the various positions adopted as the result of turnings. Plaster beds have not proved satisfactory in preventing sores in spinal-cord lesions, and their use should be condemned.

Plaster beds

To promote good circulation, frequent gentle massage to the compressed areas is essential. The skin should be kept scrupulously clean and rubbed



(*a*) (*b*) (*c*) (*d*)

FIG. 28.—Malignant sore over right trochanter in spinal-cord lesion. (*a*).—Before excision. Note extensive oedema around sore. (*b*).—Two weeks after excision. Note extent of undermined area indicated by probe. (*c*).—Eleven weeks later. (*d*).—Seven months after complete healing.

repeatedly with alcohol (50 to 60 per cent) and then dusted with powder. If the skin is harsh and dry, it is well to use a mixture of equal parts of olive oil and alcohol. Creases and crumbs in the bed-clothes must be scrupulously avoided.

General

The maintenance of a good general condition is also of vital importance in preventing bedsores.

(2) Curative

Once bedsores have developed, the principles of prophylaxis should be enforced and every effort made to remove pressure from them. In certain cases, it may be necessary to turn the patient even more frequently than every two hours.

Local treatments

Numerous local treatments for the various degrees of sore have been recommended: tulle gras, zinc oxide, scarlet red, ultra-violet irradiation, sunlight,

excision of slough; fomentations (Riddoch, 1917); sulphosalicylic acid (Drewitz, 1928); Thiocresol (Reimann, 1930); continuous water bath (Riehl, 1930); tannic acid (Latimer, 1934); elastic adhesive plaster (Carty, 1935); thymol iodide-ferrous sulphate (Fantus, 1935); zinc peroxide and sulphanilamide (Meleney and Harvey, 1939); tincture of benzoin (Tinct. Benzoini Simplex *B.P.C.*; Tinct. Benzoini *U.S.P.* XII) (Munro, 1940).

Treatment in spinal-cord lesions

The author's therapeutic tactics in bedsores of spinal-cord lesions are as follows.

First stage

Superficial sores with excoriation of skin are first cleansed with soap and water, followed by sterile sulphanilamide powder dressings, and later by Pellidol ointment 2 per cent (a non-staining compound of diacetylaminoazotoluol and soft paraffin), tulle gras or allantoin powder (*B.P.C.*). If a blister is present, the elevated epithelium is removed aseptically before the application of sulphanilamide powder.

Second stage

Superficial, indolent ulcers are scraped and the pigmented border is excised. This is followed by daily saline dressings—in certain cases alternating with penicillin solution or 0·3 per cent copper sulphate solution dressings.

Third stage

In malignant sores with penetrating gangrene, excision of the necrotic tissues and cleansing with hydrogen peroxide and saline solution or soap and water are mechanical ways of removing infecting organisms, the nature of which is ascertained by routine culture of wound swabs. Antiseptics, except penicillin, are applied to the devitalized tissue cautiously, as they have an inhibitory action on the granulations which play a vital part in the healing of deep sores in the early stages. Sores heavily infected with *Streptococcus haemolyticus*, staphylococci, *B. proteus* and *Bacillus coli* are treated with Flavazole powder (a less toxic proflavine-sulphathiazole compound) and penicillin powder for a few days, followed by saline dressings twice daily and later once daily. This local treatment is combined with a systemic intramuscular penicillin course. Those infected with *Ps. pyocyanea* are treated with 4 per cent boric acid solution or 2·4 per cent Phenoxetol (β-phenoxyethyl alcohol) solution (Berry, 1944). In later stages, when epithelization is in progress, saline dressings are alternated with Pellidol ointment or allantoin powder.

Plastic operations

In certain cases, plastic operations have proved successful in accelerating healing and also in removing scars, but in spinal-cord injuries plastic operations have proved unsuccessful and may be contra-indicated if the patient's general condition is poor.

(3) After-care

This is most important for preventing recurrence of sores, especially in complete lesions of the spinal cord and cauda equina. The patient must be trained to become "sore conscious", that is, to pay greatest attention to the bony parts in the paralysed areas of his body, once the sore is healed and he is up in a wheel-chair. He should never sit on hard surfaces, and his chair must be equipped with an air or thick Dunlopillo cushion. He should frequently (every 10 to 15 minutes) raise himself off his chair to relieve the pressed areas. On his returning to bed, these areas should be kept completely off pressure for a considerable time (at least one to two hours) and gently massaged to promote good circulation.

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[References to other titles are given under Bedsores in the Index Volume. The subject of Bedsores is also dealt with in the *British Encyclopaedia of Medical Practice* (1936), Vol. 2, p. 302.]

BERI-BERI

See SURGERY IN THE TROPICS

BILHARZIASIS

See SCHISTOSOMIASIS

BIOCHEMICAL TESTS–CURVES AND CHARTS

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1. INTRODUCTION

52.] For full advantage to be taken of biochemical tests it is necessary to appreciate their uses and limitations; much of these introductory remarks applies equally to other branches of laboratory work, including bacteriology and haematology. Except in very rare cases it is useless to attempt to make a diagnosis merely on the basis of laboratory tests; the laboratory findings form only one part, though in some cases a very important part, of the overall clinical picture, and they must be assessed together with all the other findings.

The great value of laboratory tests is that they are quantitative: for example, a properly carried out urea clearance test giving a result of 15 per cent of the normal gives a much better idea of a patient's renal condition than does any unaided clinical examination. Repeated tests at suitable intervals are much more valuable than any single test; they enable a more accurate assessment of the progress of a pathological condition to be made and assist in making a reliable prognosis.

A further important use of biochemical tests is in the control of treatment. For example, intravenous saline therapy should be controlled by frequent examination of serum chloride and, if necessary, bicarbonate level; and the dosage of oestrogen used in the treatment of prostatic cancer is regulated by the amount required to maintain the serum acid phosphatase at a normal level.

A brief, but necessarily incomplete, account of the more important biochemical tests is given in this section, but in making use of them one point should be stressed. To obtain real value from the laboratory, it should not be used as a penny-in-the-slot machine, whereby a " request form " with a specimen of blood is sent and a series of figures on a report are received in return.

Co-operation between clinician and biochemist

The clinical pathologist or biochemist in charge should be consulted in any doubtful case as to the tests most likely to be helpful, and about their interpretation in cases of difficulty; divorce of the wards from the laboratory is at best a very undesirable state, and at worst may involve great danger to the patient.

2. BLOOD SUGAR

Normal value.—The glucose content of blood is estimated by various methods, many of which are not absolutely specific and are positive for traces of other reducing substances. The fasting level varies a little according to the particular method used, but a range of 70–100 milligrams per 100 cubic centimetres covers the great majority of normal fasting blood sugars. Occasionally,

by some methods, figures as high as 120 milligrams per 100 cubic centimetres may be found, but anything above this level is abnormal.

The blood sugar varies throughout the day and values of 120–150 milligrams per 100 cubic centimetres are usually found 2–3 hours after a meal. *Diurnal variation*

Hyperglycaemia.—When the blood sugar is above the normal figures, it is most commonly due to diabetes mellitus. In mild diabetes the fasting blood sugar may be normal, although there is an abnormally high and prolonged rise following food; in more severe cases the fasting blood sugar also is raised, and very high values are sometimes met with; figures above 1,000 milligrams per 100 cubic centimetres are sometimes met with in diabetic coma. Raised blood sugars, particularly in the post-absorptive condition, are also met with in other conditions, of which thyrotoxicosis and intracranial conditions such as haemorrhage or tumour are examples.

Hypoglycaemia.—This occurs when the fasting level is below 70 milligrams per 100 cubic centimetres in starvation and in hyperinsulinism. The latter may be due to neoplasm of the islets of Langerhans, although a functional hyperinsulinism, in which no neoplasm is found, also occurs. In hyperinsulinism the blood sugar may rise normally after food or glucose, but the fall which follows is greater and more prolonged. Symptoms of hypoglycaemia usually develop at a level of about 50 milligrams. In neoplasm of the islets of Langerhans, the blood sugar may fall to extremely low values; any blood sugar less than 30 milligrams per 100 cubic centimetres on more than one occasion is sufficient justification for an exploratory laparotomy. *Pancreatic tumours*

Excretion of sugar in the urine.—Normally sugar demonstrable by the usual tests (Benedict's or Fehling's) is not found in the urine unless the blood sugar has reached a value of 180 milligrams per 100 cubic centimetres (the normal "renal threshold") or more, and the finding of glucose in the urine is presumptive evidence that the blood sugar has passed this value. Occasionally, however, individuals are found whose kidneys excrete glucose at a lower level than this, and it is necessary to differentiate them from diabetics. For this purpose a glucose tolerance test is used. The condition in which glucose is excreted with a blood sugar less than 180 milligrams per 100 cubic centimetres is known as renal glycosuria; the importance of differentiating it from diabetes is that it is a physiological abnormality which persists throughout life and requires no treatment. A true renal glycosuric subject is no more likely to develop diabetes than is an individual who excretes glucose at a normal threshold. *"Threshold" value* *Renal glycosuria*

In pregnancy the renal threshold is sometimes lowered temporarily, and there is glycosuria after meals. The blood sugar and glucose tolerance in normal pregnancy, however, fall within the usual limits. *Pregnancy*

In diabetes and in chronic nephritis the renal threshold is sometimes raised, and no sugar is excreted in the urine, even when the blood sugar is as high as 250 milligrams per 100 cubic centimetres.

3. BLOOD SUGAR CURVES

(1) Standard glucose tolerance test

The standard way of carrying out a glucose tolerance test is as follows.

The patient fasts overnight. If desired, a cup of tea (without sugar) may be

given in the early morning, but nothing to eat. At 9 a.m. the bladder is emptied, a sample of blood is taken, and 50 grammes of glucose dissolved in about 150 cubic centimetres of water are given. This may be flavoured with orange or lemon juice if desired. One-half, one, one and a half and two hours afterwards, further samples of blood are taken, and at one and two hours further specimens of urine are obtained.

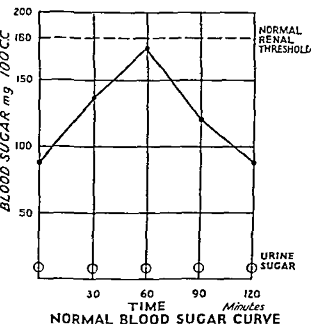


FIG. 29.—Normal blood sugar curve after 50 grammes glucose. Note: (1) fasting blood sugar is normal, (2) blood sugar does not rise above 180 milligrams per 100 cubic centimetres, (3) blood sugar returned to normal in 2 hours.

The sugar content of the blood specimens is then ascertained and the presence or absence of sugar in the urine (usually only qualitatively) is ascertained.

(2) Types of curve obtained

(*a*) *Normal curve*

The criteria of a normal glucose tolerance curve (*see* Fig. 29) are as follows.

(i) The fasting blood sugar is within the normal range given above.

(ii) The blood sugar does not at any time rise above 180 milligrams per 100 cubic centimetres.

(iii) The blood sugar has returned to normal in 2 hours.

(iv) There is no glycosuria.

(*b*) *Pathological curves*

The blood sugar curve may vary from the normal in the level of the fasting blood sugar, the amount of rise above the fasting level, delay in the return to normal and the presence of glycosuria.

(*c*) *Renal glycosuria*

This has been referred to above. In this condition the fasting blood sugar, the rise and return to normal are all within normal limits, but sugar is excreted in the urine. The level of blood sugar at which this occurs varies in different subjects, and in extreme cases glycosuria may occur with a blood sugar as low as 100 milligrams per 100 cubic centimetres. The importance of knowledge of this condition is in its differentiation from diabetes.

(*d*) "*Lag storage*" *curve*

In this type of curve (Fig. 30) the fasting blood sugar is normal, but the blood sugar after the administration of glucose rises above 180 milligrams per 100 cubic centimetres, although it returns to normal within the usual time of 2 hours. There is usually glycosuria at the time of the high blood sugar. This type of curve is indicative of abnormally rapid absorption of glucose. It

occurs in a normal individual if the glucose is administered through a duodenal tube, and is frequently found if a glucose tolerance test is carried out on a patient with a gastro-enterostomy. The importance of this, again, is that it is not a diabetic condition and requires no treatment.

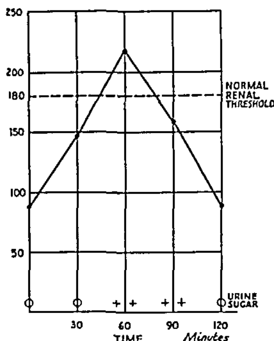


Fig. 30.—"Lag storage" curve. Blood sugar rises above 180 milligrams per 100 cubic centimetres, but has returned to normal in 2 hours.

(e) *"Flat" curve*

This is the opposite condition to that illustrated by the "lag storage" type of curve. The fasting blood sugar is normal, but the rise after the test dose is less than normal, and usually less than 40 milligrams per 100 cubic centimetres. This type of curve is characteristic of idiopathic steatorrhoea of various forms, for example, sprue, non-tropical sprue and coeliac disease. It also occurs, though not constantly, in certain endocrine disorders such as hypopituitarism (Simmonds's disease) and Addison's disease.

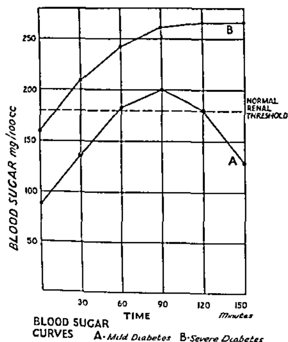


Fig. 31.—Blood sugar curves in diabetes. A—mild, B—severe. In A fasting blood sugar is normal, the rise is only slightly greater than normal, but the value is still much above normal in 2 hours. In B the curve is abnormal throughout.

(f) *Diabetic type*

In mild diabetes the fasting blood sugar is normal, but the rise after 50 grammes of glucose is greater than normal, and the return to normal takes longer than 2 hours (*see* Fig. 31). The delay in the return to normal is more important than the actual maximal blood sugar level reached. In more severe

diabetes the fasting blood sugar is greater than normal, the rise higher and the return towards normal still slower, and in really severe cases the fasting level may be 300 milligrams per 100 cubic centimetres or more, and the blood sugar may still be rising after 2 hours.

Other causes of diabetic type of curve

This type of curve is characteristic of diabetes mellitus, but the milder degrees of abnormality are met with in many other conditions; chronic sepsis and overwork produce temporary impairment of glucose tolerance, and the same is true of certain endocrine disorders, notably acromegaly and hyperthyroidism. Operative treatment of acromegaly and hyperthyroidism produces an improvement in the glucose tolerance, frequently to normal. Certain other intracranial conditions, such as cerebral haemorrhage or tumour, also produce a diabetic type of curve.

A mild diabetic type of curve is readily produced in a normal individual by a very low carbohydrate diet for a few days; consequently, an abnormal sugar tolerance in a starving patient must not be regarded as diagnostic of diabetes.

4. RENAL FUNCTION

An enormous number of tests have been proposed for the investigation of renal function, but this section is limited to the discussion of blood urea, urea concentration test, urea clearance test and concentration and dilution tests, as these are in general the most useful and most widely used. The microscopical examination of urinary deposit must, of course, not be omitted in any case in which it is necessary to investigate renal function.

(1) Blood urea

Normal level.—The level of blood urea remains nearly constant throughout the day, and is not affected by ordinary meals. Over a period of days, a high protein or a low protein diet does affect the level of blood urea, and the previous diet may have to be considered when interpreting a blood urea determination. The range of normal blood urea for patients on an ordinary diet is some 25–40 milligrams per 100 cubic centimetres. In childhood or old age, values of over 40 milligrams per 100 cubic centimetres are met with occasionally, and in pregnancy the normal range is much lower, usually 15–25 milligrams per 100 cubic centimetres. Any value above 30 milligrams per 100 cubic centimetres in a pregnant woman is to be regarded with suspicion.

Pregnancy

The only condition in which an abnormally low blood urea occurs is that of the terminal stages of hepatic failure, when failure to deaminate amino acids may lead to an accumulation of amino acids in the blood and a fall in the urea.

High blood urea.—Apart from pure renal failure, the causes of raised blood urea are very numerous. From the surgical point of view, the most important of these is obstruction to the urinary passages, as for example from an enlarged prostate or a calculus, the immediate result of which is a rapidly rising blood urea, which may reach very high values—300 milligrams per 100 cubic centimetres or more. Although the rate of increase of blood urea depends very much upon diet, the author has seen the blood urea rise at the rate of about 40 milligrams per 100 cubic centimetres *per diem* in some cases of anuria. Similarly high values are met with in severe dehydration, as in repeated vomiting or very profuse diarrhoea. The very high blood urea figures

Urinary obstruction

sometimes seen in alkalosis are due to dehydration rather than to the change in the acid-base balance, and blood urea rapidly falls when dehydration is relieved, even though the blood chemistry is still abnormal.

Some rise in blood urea up to 60–80 milligrams per 100 cubic centimetres is also commonly met with in congestive cardiac failure. Most of these cases of "extrarenal uraemia" can be differentiated from true uraemia due to chronic nephritis by the fact that the urine is concentrated, with a urea content of 3–4 per cent, whereas the true uraemic has a dilute urine with a very low urea content. *"Extrarenal uraemia"*

(2) Non-protein nitrogen (N.P.N.)

In some laboratories this determination is used instead of that of blood urea as a guide to nitrogen metabolism. In ordinary clinical work, these are alternatives, and no advantage is gained by carrying out both tests. The nitrogen content of urea is just under 50 per cent, but in normal blood the other non-protein-nitrogenous compounds, uric acid, creatinine etc. make the N.P.N. value nearly as high as the blood urea, and 25–35 milligrams per 100 cubic centimetres covers the majority of normals. In conditions of gross nitrogen retention, in which urea is the principal constituent, N.P.N. values are somewhat over half the urea value, for example, a blood urea of 300 milligrams per 100 cubic centimetres may give an N.P.N. figure of say 160–170 milligrams per 100 cubic centimetres.

(3) Urea clearance test

This is the most satisfactory test for renal function, and provided that care is taken in collecting *complete* urine specimens, it is very reliable. It can be used with perfectly consistent results even after a suprapubic cystotomy.

Method of carrying out the test.—No special preparation of the patient is required.

Urine is collected at 10 a.m., 11 a.m. and 12 noon; the bladder must be completely emptied each time, using a catheter if necessary. The exact time each specimen of urine is passed *must be noted to the nearest minute*; the whole of the 11 a.m. and 12 noon specimens, each representing one hour's urine, is sent to the laboratory. Each specimen must be clearly labelled with the *exact* times of the beginning and end of the period of collection. It is not important that the specimens should be accurate hourly ones, but the test is useless unless the exact times are noted on each specimen.

Blood must be taken for blood urea estimation between 10.45 a.m. and 11.15 a.m. and sent to the laboratory with the urine specimens.

Interpretation of results.—It has been mentioned already that the blood urea level depends largely upon the patient's diet; thus a normal individual on a low protein diet may have a blood urea of 20 milligrams per 100 cubic centimetres whereas the same individual on a high protein diet may have one of 45 milligrams per 100 cubic centimetres. A nephritic patient may have a value of 40 milligrams per 100 cubic centimetres on the low protein diet which he is probably taking, whereas a high protein diet would produce a value of, say, 80 milligrams per 100 cubic centimetres. Consequently, a blood urea finding of 40 milligrams per 100 cubic centimetres is of limited significance, unless the patient's diet is fairly well known. The urea clearance test takes the

effect of diet into consideration by measurement of the urinary excretion of urea.

It is found experimentally that with normal kidneys, if the amount of urine exceeds about 2 cubic centimetres per minute (the "augmentation limit"), the amount of urea excreted per minute is equal to the urea content of 75 cubic centimetres of blood. With a diuresis of less than 2 cubic centimetres per minute, the urea excretion is less, proportionately to the square root of the urine volume; thus, reducing the urine output to 0·5 cubic centimetre per minute halves the amount of urea excreted. To obtain comparable results in different cases, the "standard urea clearance" is calculated from a formula which reduces the diuresis to a standard value of one cubic centimetre per minute. The result is expressed as the "number of cubic centimetres of blood cleared of urea per minute" by the kidneys.

The normal "standard urea clearance" is 54 cubic centimetres per minute, but variations from 75–125 per cent of this value are within normal range. When a diuresis of more than 2 cubic centimetres per minute occurs, the method of calculation is different, and the normal value for the "maximum urea clearance" is taken as 75 cubic centimetres per minute, but the normal range is again 75–125 per cent of this value.

Sometimes a low value for the urea clearance is found with normal kidneys, owing to the great reserve which they possess. In such a case, with a low blood urea, the urea clearance should be determined again, after 15 grammes of urea in 200 cubic centimetres of water have been given, when the value is usually raised to the normal range. This is never necessary if the blood urea, before urea has been given, is 45 milligrams or more per 100 cubic centimetres.

Prognosis value

In nephritis, very low values for the urea clearance may be found, during the acute phase, without in any way necessitating a bad eventual prognosis, but when the clearance has fallen to a permanent value less than 20 per cent of normal, two-thirds of the patients die within a year, the remaining third within two years. Uraemic symptoms are usually absent as long as the urea clearance is greater than 10 per cent of normal, and are practically always present when the clearance is less than 5 per cent.

In the case of children, the actual findings are adjusted for the size of the patient by a correction factor depending upon the body size.

(4) Urea concentration test

This is still a widely used test, although greater information is obtained with less trouble from a urea clearance.

The test is carried out by emptying the bladder completely, drinking a solution of 15 grammes of urea in 100 cubic centimetres of water and emptying the bladder again one, two and three hours after the urea has been taken. The *whole* of all four specimens should be sent to the laboratory. The test is carried out first thing in the morning, and the patient must not have had anything to drink since the previous evening.

Interpretation.—A normal kidney will usually excrete urine containing more than 2·5 per cent urea in at least one specimen; it is immaterial which one; even the pre-urea specimen may be highest. Frequently, values of over 3 per cent are found, and values less than 2 per cent are very strongly suggestive of impaired renal function.

If there is a diuresis of more than about 100 cubic centimetres in any hour, a low finding is not necessarily due to renal insufficiency, and the test should be repeated.

(5) Concentration and dilution tests

A concentration-dilution test is one of the simplest renal function tests, and can be performed without any laboratory facilities, a measuring cylinder and urinometer being all the apparatus required.

(i) *Concentration test.*—The patient takes a high protein supper, with a limited amount of drink, in the evening; he empties the bladder completely before retiring; any urine passed during the night is discarded. On waking, the patient passes urine and the specimen is saved and labelled "1"; one hour later, a further specimen "2" is passed.

(ii) *Dilution test.*—1,500 cubic centimetres of water is then drunk within half an hour. The bladder is then emptied at ½ to 1 hour intervals for 4 hours, and the specimens are labelled "3", "4" and so on.

The specific gravity and volume of each specimen is determined.

(iii) *Interpretation.*—In a normal subject, the specific gravity of one of the specimens "1", "2" should be 1·028 or more, and that of the later specimens should fall considerably below 1·010, usually to 1·002 or 1·003. Further, the greater part of the 1,500 cubic centimetres of fluid should be excreted within 3–4 hours.

In some patients, the excretion of water may be delayed, either from renal deficiency, or for other reasons, such as cardiac failure or oedema from other causes. In these circumstances the concentration test still gives normal or nearly normal results in patients with healthy kidneys, whereas in renal deficiency both the concentration and dilution tests are seriously interfered with. In the late stages of nephritis, there is a tendency for fixation of the urine specific gravity at about 1·008 to 1·010 throughout both tests.

5. JAUNDICE AND LIVER FUNCTION

On account of the multiplicity of function and the reserve power of the liver and because its secretion, the bile, cannot, unlike the urine, be obtained uncontaminated and quantitatively, liver function tests are much more subject to limitations than are renal function tests. *Limitations*

Jaundice is one of the most obvious signs of liver abnormality and will be considered first, followed by notes on a selection of the numerous tests which have been devised for examination of the other functions of the liver.

(1) Bilirubin metabolism

Bilirubin is produced mainly by the breakdown of haemoglobin by the reticulo-endothelial system, largely in the Kupffer cells of the liver, and is excreted by the epithelial cells of the liver into the bile. In the intestine, the bilirubin is reduced to urobilin (sometimes the faecal urobilin is termed stercobilin); part of this urobilin is excreted in the faeces, and part is reabsorbed. Of the reabsorbed portion the greater quantity is re-excreted by the liver, but traces escape in the urine. An understanding of this brief physiological introduction is fundamental in the differential diagnosis of various forms of jaundice.

(i) *Blood bilirubin.*—Normal serum contains small quantities of bilirubin, usually below 0·5 milligram per 100 cubic centimetres, though some authors give higher figures as the upper limit of normal, even as high as 1·7 milligrams. Any value above 1 milligram should be regarded with suspicion. The blood bilirubin is measured either as the "icterus index", which is a simple colorimetric comparison of the colour of the serum with a standard (the normal value is usually 4–6 units) or by means of the van den Bergh reaction in which the serum is treated with van den Bergh's reagent and develops a colour. The result of this test is frequently expressed in units. One unit is equivalent to 0·5 milligram per 100 cubic centimetres.

"Icterus index"

Van den Bergh reaction

The van den Bergh reaction gives two types of result. Some sera give a colour directly on the addition of the reagent; this is described as a *direct reaction.* Other sera require the addition of alcohol before the colour is developed, and this is described as an *indirect reaction.* The bilirubin in normal sera always gives an indirect reaction.

In the earlier days of the test, "biphasic" and "delayed direct" reactions were described, and diagnostic value was attributed to them in the differentiation of various forms of jaundice. However, all modern workers agree that these are merely modifications of the direct reaction and have in themselves no diagnostic significance.

(ii) *Hyperbilirubinaemia (jaundice).*—The maintenance of serum bilirubin at a normal level depends upon the approximate constancy of the rates of production and excretion, and a rise in serum bilirubin can be produced either by excessive production or by diminished excretion, or sometimes by the two together.

The three main causes of jaundice are as follows.

(1) Excessive production of bile pigment (haemolytic jaundice).

(2) Damage to liver cells and fine bile passages, making them unable to excrete normal amounts of bile pigment (toxic, infective, hepatogenous jaundice).

(3) Obstruction to larger bile ducts (obstructive jaundice).

(2) Galactose and laevulose tolerance tests

(*a*) *Galactose tolerance test*

The old galactose tolerance test consisted of giving 40 grammes of galactose by mouth and collecting the urine for 5 hours. The excretion of more than 3 grammes of galactose was reckoned a positive result. This test has been superseded by methods in which the galactose content of the blood is estimated after a test dose. Two main forms of the test are used.

(i) *The oral test.*—Forty grammes of galactose in 250 cubic centimetres of warm water are given to the fasting patient; the blood is taken ½, 1, 1½ and 2 hours afterwards. The blood galactose is estimated in all four specimens, and the "galactose index" is calculated by adding together the four blood galactose values. The normal "galactose index" is less than 160 (110 for healthy medical students) and the maximal blood galactose is less than 80 milligrams per 100 cubic centimetres.

(ii) *The intravenous test.*—Fifty cubic centimetres of sterile 50 per cent galactose solution is injected intravenously. Blood is taken 2 hours later.

With normal liver function, blood galactose is below 10 milligrams per 100 cubic centimetres at this time.

(*b*) *Laevulose tolerance test*

Laevulose tolerance tests, in which alterations in total blood sugar are observed following ingestion of 50 grammes of laevulose, are of limited value as the variation in blood sugar is not entirely due to laevulose.

The laevulose tolerance is of much greater value if blood laevulose is estimated usually half-hourly for 2 hours following 50 grammes of laevulose by mouth. Normally the maximal rise occurs within the first hour, and with a normal liver should not exceed 20 milligrams per 100 cubic centimetres (usually 15 milligrams or less), and the value should have fallen to 8 milligrams per 100 cubic centimetres or less in 2 hours.

Interpretation.—The galactose and laevulose tests can be discussed together. Of the two the galactose test is probably the more reliable. They give positive results in cases in which there is parenchymatous damage in the liver, and the figures are roughly proportional to the extent of damage. Thus, an obstructive jaundice may give normal results at first, but positive results later as the liver cells become damaged. Similarly, although in many cases of cirrhosis there are positive results, sometimes the hypertrophy of the surviving hepatic tissue produces normal results. Toxic hepatitis gives almost invariably positive results which return to normal as the condition improves. *Obstructive jaundice* *Toxic hepatitis*

(3) Flocculation tests

A number of tests have been devised which consist in the production of precipitation or flocculation when the serum is mixed with the reagent solution. Among these may be cited the Takata-Ara, serum colloidal gold, cephalin-cholesterol and thymol turbidity tests. These probably depend upon changes in the γ-globulin of the serum.

The Takata-Ara test gives nearly uniformly positive results in cirrhosis. *Cirrhosis* The other tests are of greater value in the diagnosis of jaundice; although they vary in detail, they may be summed up together as giving, in general, positive results with toxic hepatitis, and negative ones with obstructive jaundice. Of these the thymol turbidity test is technically much the easiest, and therefore probably preferable for routine purposes.

(4) Hippuric acid synthesis tests

These are among the most satisfactory tests for estimating hepatic function. Sodium benzoate is administered, and the amount conjugated in the liver with glycine and excreted in the urine as hippuric acid is measured. The sodium benzoate is usually given orally, but some workers prefer intravenous administration.

(i) *The oral test.*—No drugs must be given for two days before the test. One hour after breakfast, 6 grammes of sodium benzoate in 30 cubic centimetres water flavoured with peppermint is given and followed by half a glassful of water. The bladder is emptied immediately, the urine is collected hourly for four hours, and the whole of all four hourly specimens sent to the laboratory.

(ii) *The intravenous test.*—Twenty cubic centimetres of an 8·85 per cent solution of sodium benzoate in water are injected intravenously, at least five

minutes being taken over the injection. The bladder is emptied immediately, and one hour later. The whole *one-hourly* specimen is sent to the laboratory. Diuresis is assured by giving one pint of water to drink just before the injection.

(iii) *Interpretation.*—The normal adult excretes 3–3·5 grammes of benzoic acid (as hippuric acid) in four hours in the oral test. In hepatic insufficiency lower excretions are met with, and an excretion of less than two grammes in a jaundiced patient suggests a poor operative risk. Anaesthesia produces a sharp fall in the functional capacity of the liver as measured by this test. This fall can be lessened by the administration of carbohydrate. It should be noted that low values are also shown by the test in patients who have normal livers but renal insufficiency. In cases of doubt a urea clearance test should be carried out simultaneously.

Operability of jaundiced patients

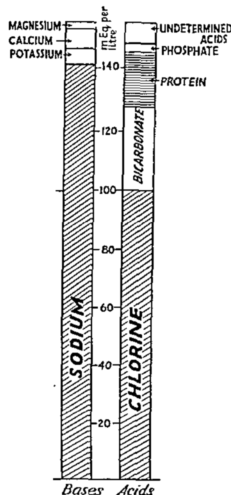


FIG. 32.—Salt composition of normal serum. Note preponderance of sodium among the bases, and of chlorine and bicarbonate among the acids.

The normal value for the intravenous test is 0·7–1·0 gramme of benzoic acid excreted in one hour. The factors producing low results are the same as in the oral method.

(5) Other metabolic changes in liver disease

(i) *Plasma or serum proteins.*—The liver seems to be the principal source of plasma protein, and parenchymatous change in the liver interferes with its synthesis, particularly that of albumin. The consequence is a tendency to a low total plasma protein and a reversal in the albumin : globulin ratio, the fall in albumin being particularly marked, for example 5 grammes per 100 cubic centimetres total protein, with 1·8 grammes of albumin and 3·2 grammes of globulin. Sometimes the total value is within the normal range, but the albumin: globulin proportions are still reversed, for example 6·5 grammes per 100 cubic centimetres of total protein with 2·3 grammes of albumin and 4·2 grammes of globulin. The diminution of albumin with reversal of the albumin : globulin ratio is practically constant in hepatic cirrhosis. It also occurs in other hepatic diseases such as toxic hepatitis and carcinomatosis, but not so constantly as in cirrhosis (*see* p. 93).

A:G ratio in cirrhosis

The low protein level and oedema of cirrhosis cannot be remedied by a high protein diet owing to inability of the liver to manufacture new serum protein, but they are sometimes relieved by intravenous administration of plasma.

The fibrinogen of the plasma falls in such severe conditions as acute yellow atrophy, but is usually normal (0·2–0·4 per cent) in the majority of liver diseases. *Acute yellow atrophy*

(ii) *Cholesterol.*—The serum or plasma cholesterol occurs in two forms, free cholesterol and cholesterol esters. The normal range is about 100–250 milligrams per 100 cubic centimetres for total cholesterol, about half being in the form of ester. In the majority of laboratories total cholesterol only is estimated.

In obstructive jaundice, both cholesterol fractions are increased, roughly parallel with the degree of jaundice, and on relief of the obstruction the value slowly returns to normal. In very long-standing jaundice the level gradually falls, concomitantly with liver degeneration.

In parenchymatous liver disease, the total value is normal, or in long-standing disease it is low, and the fall principally affects the ester fraction. In some severe cases of hepatitis, the cholesterol esters practically disappear. In cirrhosis there is no striking change except in the terminal stages, when there is sometimes a fall.

Cholesterol determinations are of no value in the diagnosis of gall-stones.

(iii) *Serum phosphatase.*—The alkaline phosphatase is usually raised in obstructive jaundice, but is usually normal in jaundice due to toxic hepatitis. This difference is sometimes of value, together with other evidence, in helping in the differential diagnosis of the two conditions, but is not sufficiently constant to be relied upon alone. In cirrhosis the phosphatase is frequently, though not always, raised. *Obstructive jaundice*

(6) Selection of tests

With such a galaxy of available tests it is difficult to choose the best tests in various conditions. The following suggestions may be helpful.

(*a*) *Diagnosis of jaundice of unknown origin*

The best aids to diagnosis are the van den Bergh reaction, examination of the urobilin excretion, the thymol turbidity test and assessment of the alkaline phosphatase. If the thymol test is negative and the alkaline phosphatase above 35 units, biliary obstruction is practically certain. A positive thymol test with phosphatase below 25 units is against this diagnosis. A galactose or laevulose tolerance test sometimes helps. A normal result is against the diagnosis of toxic hepatitis. *Biliary obstruction*

(*b*) *Prognosis and assessment of operative risk*

The hippuric acid test is the most generally useful. Serum protein estimations are also of some prognostic value. Estimation of prothrombin time is also of importance in assessing the liability to haemorrhage in jaundiced patients, especially as a deficiency of prothrombin can readily be treated by vitamin K.

6. ACID-BASE BALANCE

Space does not permit discussion of the complete bodily mechanisms for regulating acid-base balance, and in this section will be considered principally the information given by examination of the blood in disturbances of the acid-base equilibrium.

minutes being taken over the injection. The bladder is emptied immediately, and one hour later. The whole one-hourly specimen is sent to the laboratory. Diuresis is assured by giving one pint of water to drink just before the injection.

(iii) *Interpretation.*—The normal adult excretes 3–3·5 grammes of benzoic acid (as hippuric acid) in four hours in the oral test. In hepatic insufficiency lower excretions are met with, and an excretion of less than two grammes in a jaundiced patient suggests a poor operative risk. Anaesthesia produces a sharp fall in the functional capacity of the liver as measured by this test. This fall can be lessened by the administration of carbohydrate. It should be noted that low values are also shown by the test in patients who have normal livers but renal insufficiency. In cases of doubt a urea clearance test should be carried out simultaneously.

Operability of jaundiced patients

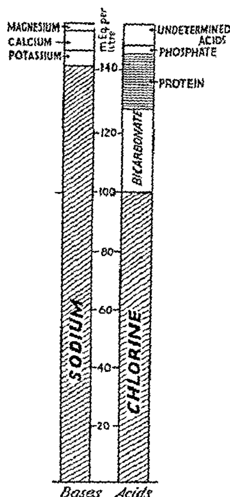


FIG. 32.—Salt composition of normal serum. Note preponderance of sodium among the bases, and of chlorine and bicarbonate among the acids.

The normal value for the intravenous test is 0·7–1·0 gramme of benzoic acid excreted in one hour. The factors producing low results are the same as in the oral method.

(5) Other metabolic changes in liver disease

(i) *Plasma or serum proteins.*—The liver seems to be the principal source of plasma protein, and parenchymatous change in the liver interferes with its synthesis, particularly that of albumin. The consequence is a tendency to a low total plasma protein and a reversal in the albumin: globulin ratio, the fall in albumin being particularly marked, for example 5 grammes per 100 cubic centimetres total protein, with 1·8 grammes of albumin and 3·2 grammes of globulin. Sometimes the total value is within the normal range, but the albumin: globulin proportions are still reversed, for example 6·5 grammes per 100 cubic centimetres of total protein with 2·3 grammes of albumin and 4·2 grammes of globulin. The diminution of albumin with reversal of the albumin : globulin ratio is practically constant in hepatic cirrhosis. It also occurs in other hepatic diseases such as toxic hepatitis and carcinomatosis, but not so constantly as in cirrhosis (*see* p. 93).

A:G ratio in cirrhosis

The low protein level and oedema of cirrhosis cannot be remedied by a high protein diet owing to inability of the liver to manufacture new serum protein, but they are sometimes relieved by intravenous administration of plasma.

If fluid is lost from the body, as in vomiting or diarrhoea, in diabetic coma or in Addison's disease, sodium and chlorine are also lost, though in varying proportions in the various conditions. This leads to characteristic changes in the acid-base pattern of the serum.

The amounts of sodium, chlorine etc. in serum are expressed in milli-equivalents per litre, instead of the more common milligrams per 100 cubic centimetres. It is impossible to add so many "milligrams" of chlorine to "volumes" of bicarbonate and "per cent" of protein and get a rational answer. The milli-equivalent of any substance is merely its equivalent weight in milligrams, and is obtained by dividing the number of milligrams of substance in 1 litre by the equivalent weight; for example, serum normally contains some 355 milligrams of chlorine per 100 cubic centimetres, or 3,550 milligrams per litre. If this is divided by 35·5 (the atomic weight of chlorine) it gives a value of 100 milli-equivalents per litre. This also obviates the confusion which arises through uncertainty as to whether a chlorine value is expressed as chlorine or as sodium chloride. If the serum chlorine value is expressed as 585 milligrams (as sodium chloride) per 100 cubic centimetres, then the division has to be made by 58·5 (molecular weight of sodium chloride), which gives the same answer. The conception is used in everyday parlance in connexion with test meals; the expression of x cubic centimetres N/10 per cent is merely a rather clumsy way of saying x milli-equivalents per litre.

Conversion figures for some of the more important electrolytes are shown below.

	Mean normal value as often expressed	Value per litre	Divide by equiv. wt.	Mean normal value in m.-Eq. per lit.
Chlorine (as chlorine) ..	355 mgm./100 c.c.	3,550 mgm.	35·5	100
(as sodium chloride)	585 mgm./100 c.c.	5,850 mgm.	58·5	100
Sodium	325 mgm./100 c.c.	3,250 mgm.	23·0	141
Bicarbonate	60 c.c./100 c.c.	600 c.c.	22·3	27

Fig. 33 shows the composition of various typical pathological sera. In this figure, for simplicity, only total base and not its separate constituents is shown, and among the acids, protein, phosphate and other ions are grouped together as "R".

Alkalosis and vomiting

In vomiting due to pyloric stenosis, fluid containing a little sodium chloride but much hydrochloric acid is lost. The initial result is a fall in the chlorine content of the serum, which is replaced by bicarbonate, thus producing alkalosis. At first the sodium level does not show great changes, but if the vomiting continues, the reserves in the extracellular fluids are insufficient to maintain this level, and the serum sodium begins to fall. By the time there is a significant fall in the serum sodium there is usually serious dehydration and a rise in blood urea, sometimes to quite high levels.

Lower bowel obstruction

In vomiting due to obstruction lower down and in profuse diarrhoea, the essential picture is similar, but the fall in chlorine and its replacement by bicarbonate is less marked, as the vomitus or dejecta are less acid than the gastric contents vomited in a case of pyloric stenosis.

Diabetic ketosis

Nephritis

In diabetic ketosis, the principal initial change is a fall in the bicarbonate, which is replaced by ketone acids, but in the later stages there is a fall also in sodium and chlorine. In the acidosis of nephritis a fall in the bicarbonate is replaced by an accumulation of phosphate and undetermined acid radicals.

In Addison's disease, the primary effect is a fall in serum sodium, through lack of renal tubular reabsorption in the absence of suprarenal cortical hormone; the loss of chloride and bicarbonate is that corresponding to the fall in sodium.

Normal serum contains as bases sodium, potassium, calcium and magnesium, and these are neutralized by chloride, bicarbonate, phosphate, protein and small amounts of other ions. It is essential to realize at the beginning that changes in these blood constituents are not independent happenings, but that a change in one necessitates compensatory changes in others.

Interdependence of changes

Fig. 32 illustrates the composition of normal serum and demonstrates graphically the overwhelming quantitative importance of sodium, chlorine

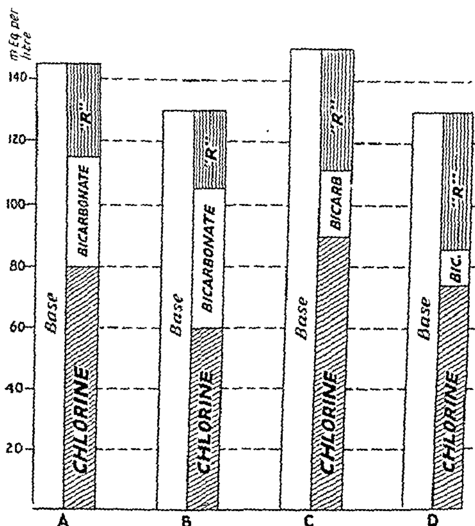


FIG. 33.—Salt composition of pathological sera. A and B—mild and severe degrees of alkalosis as in vomiting following pyloric obstruction; C and D—mild and severe degrees of acidosis as in uraemia or diabetic ketosis. In the diabetic conditions a large amount of "R" is accounted for by ketone bodies (acetoacetic and hydroxybutyric acids). In B and D the most important change is the fall in total base level.

and bicarbonate ions in the acid-base balance of the blood. Sodium is the principal base and chloride the principal acid ion throughout the extracellular fluids of the body, and changes in these are closely connected with changes in the extracellular fluids in general. Potassium occurs only in small amounts in the extracellular fluids and serum, though it is the principal base in the cells.

There is no real advantage in using fluids other than sodium chloride solution in most cases; the normal kidney will excrete whichever ion is offered in excess of the body requirements. Occasionally, in spite of large quantities of saline, difficulty may be found in restoring the blood chemistry to normal. In some of these patients, particularly with malignant disease of the gastro-intestinal tract, a low serum protein content is found, and if plasma is given to restore this the subsequent effect of saline may be more successful.

Choice of replacement fluid

A word of warning, however, is necessary in dealing with young infants, up to a year or so old. The kidneys of these infants are capable of concentrating salts only to a very limited extent, and if prolonged parenteral saline therapy is needed after the initial suspected loss of body fluid has been replaced by *normal* saline, much weaker salt solutions (for example, 0·2 per cent NaCl with 4 per cent glucose) should be continued to avoid the risk of salt poisoning.

Precautions with infants

7. TEST MEALS

In the majority of conditions, fractional test meals give disappointingly little information, especially when the trouble involved in obtaining satisfactory specimens and examining them is considered. This is due (a) to the very wide range of normal findings and (b) to the inconstancy of changes in particular types of disease.

(1) Types of test meal

Three types of test meal are popular.

(i) The classical test meal of thin gruel (2 tablespoonsful of oatmeal in a quart of water without salt, boiled down to a pint).

(ii) The alcohol test meal: 50 cubic centimetres of 7 per cent alcohol containing 1 cubic centimetre of 1 per cent phenolphthalein solution is the most widely used alcohol meal.

(iii) The histamine test: 0·5 milligram of histamine is injected subcutaneously and the gastric contents are collected.

The details of passing a Ryle's tube are omitted, but it is essential to make sure that the tip of the tube is in the stomach. This usually requires passing some 20–24 inches in the normal subject, though many patients fall outside this range. Specimens are collected, after the whole of the fasting contents have been aspirated, at varying periods; specimens taken every half-hour for three hours give as much information as do more frequent ones.

(2) Fasting juice

The normal fasting stomach contents have a volume usually of between 20 and 100 cubic centimetres; the free hydrochloric acid content is usually between 0 and 40 cubic centimetres N/10 acid per cent; lactic acid and starch are absent, and blood, if present, is only in minute traces due to passage of the tube. Mucus is normally present only in traces; the presence or absence of bile is without significance.

In pyloric obstruction due to simple stenosis or carcinoma, the contents are sour-smelling, the volume is much greater, free hydrochloric acid is low or absent, starch and lactic acid are abundant and, particularly in carcinoma, altered blood may be present. It cannot, however, be too strongly emphasized

In many of these conditions there may be a rise in the potassium content of serum at the same time as a fall in the sodium, for which this rise, however, is never sufficient to compensate osmotically. Even a rise of 50 per cent in serum potassium from 20 milligrams per 100 cubic centimetres to 30 milligrams per 100 cubic centimetres corresponds to a rise of only 2·5 m.-Eq. per litre, while the fall in sodium may be 30 m.-Eq. per litre or sometimes even more.

Significance of changes in sodium, chlorine and bicarbonate.—In general the body is remarkably tolerant of changes in the *relative* proportions of the radicals in the serum, but is remarkably intolerant of change in the *total* salt content. Although dehydration and salt loss are experimentally different conditions, in clinical practice they go closely together, and it is not usually till a condition of serious dehydration has arisen that the serum sodium begins to fall significantly. A low serum sodium value is very strong evidence that the fluids of the body are greatly depleted and that fluid and salt are urgently required.

Dehydration

In clinical practice, determination of serum sodium is rather laborious and time-consuming, but if the interrelationship of the various ions is remembered, information as to the patient's metabolic condition can be obtained by estimation of the chlorine and bicarbonate in the serum, and of the blood urea. In the surgical conditions previously referred to, a rise in the blood urea is indicative of dehydration, and a fall in the sum of the chloride and bicarbonate to below 125 m.-Eq. per litre is strongly suggestive of a fall in serum total base.

Raised levels of sodium and chlorine occur but rarely. The conditions in which they occur are usually associated with dehydration and frequently with some intracranial condition. A large proportion of these cases of sodium and chloride retention are complicated by a renal abnormality whereby little or no chloride is excreted in the urine, and they can be detected only by chemical examination of the blood. However, there is small risk of producing salt retention in an adult by intravenous saline if reasonable care is used.

Oliguria and dehydration

Examination of the urine is often helpful in assessing the patient's condition. *Persistent oliguria, under 600 cubic centimetres a day with a concentrated* urine, is evidence of dehydration, although in suprarenal insufficiency there may be marked fall in blood electrolytes with a large urinary volume. It is important to realize that in very severe dehydration the urine is nearly always acid, even when there is marked alkalosis in the tissues. Frequently a patient with alkalosis due to vomiting caused by pyloric stenosis passes a strongly acid urine, which rapidly becomes alkaline as intravenous saline therapy begins to take effect.

The treatment of these conditions is described in another section, but certain general observations are relevant here. It is necessary to replace not only the water which the body lacks, but also the salts. If there is serious deficit of salts (for example, if the sum of chloride + bicarbonate ion is less than 125 m.-Eq. per litre) it is frequently advantageous to start with salt solution about twice the normal strength (say 2 per cent of NaCl) and then to continue with normal saline until the blood chemistry is normal. The blood urea will frequently fall to normal as the dehydration is relieved, and a normal blood urea is no indication that the normal blood electrolyte composition has been restored.

There is no real advantage in using fluids other than sodium chloride solution in most cases; the normal kidney will excrete whichever ion is offered in excess of the body requirements. Occasionally, in spite of large quantities of saline, difficulty may be found in restoring the blood chemistry to normal. In some of these patients, particularly with malignant disease of the gastro-intestinal tract, a low serum protein content is found, and if plasma is given to restore this the subsequent effect of saline may be more successful. *Choice of replacement fluid*

A word of warning, however, is necessary in dealing with young infants, up to a year or so old. The kidneys of these infants are capable of concentrating salts only to a very limited extent, and if prolonged parenteral saline therapy is needed after the initial suspected loss of body fluid has been replaced by *normal* saline, much weaker salt solutions (for example, 0·2 per cent NaCl with 4 per cent glucose) should be continued to avoid the risk of salt poisoning. *Precautions with infants*

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Findings in gastric carcinoma

that in the early stages of carcinoma of the stomach the fasting gastric contents and even the response to a test meal *may* be absolutely normal, and that to wait to make the diagnosis until the sour-smelling obstructive contents are obtained is nearly always to wait until the disease is inoperable. The presence of lactic acid merely denotes pyloric obstruction and in no way differentiates between simple and malignant obstruction.

(3) Fractional test meals

The specimens are usually examined for free hydrochloric acid and total acid content, presence of bile, mucus and blood, and for persistence of starch

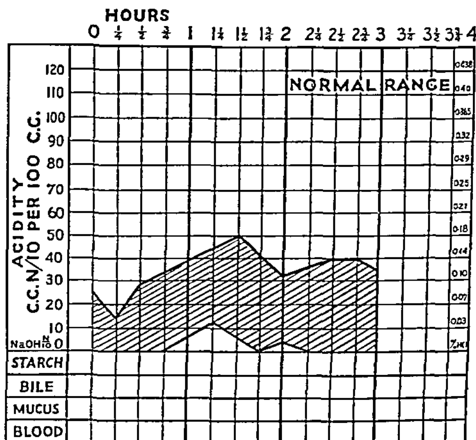


FIG. 34.—Fractional test meal. Shaded area shows range for free HCl in the majority of normal subjects.

(in a gruel meal) or phenolphthalein (in an alcohol meal) as an indication of the emptying time. The curves obtained with gruel and alcohol are usually closely similar. Fig. 34 shows the range for free hydrochloric acid within which the *majority* of normals fall, though it must be realized that some normal individuals fall outside the range. The "total acid" curve in a normal meal usually lies about 5–10 cubic centimetres N/10 acid per cent above the curve for free hydrochloric acid. The emptying time is usually about two hours.

It is impossible to describe any curves as diagnostic of any particular condition, as there is such a very considerable variation in the findings in most diseases. Among the most consistent findings in disease, subject to many exceptions, are the prolonged high acid curve with delayed emptying seen

frequently in duodenal ulcer, and the achlorhydria with fairly high total acid (due to lactic acid) often met with in the late stages of carcinoma. *Duodenal ulcer*

In pernicious anaemia there is always a complete achlorhydria which is resistant to histamine, in contradistinction to the achlorhydria of chronic gastritis, which usually responds to histamine by secretion of hydrochloric acid. The demonstration of a histamine-fast achlorhydria in a patient suspected of pernicious anaemia is the most valuable function of test meals in clinical medicine or surgery. *Achlorhydria*

8. MISCELLANEOUS BIOCHEMICAL TESTS

(1) Amyloid

The presence of amyloid disease can be demonstrated by the capacity of amyloid material to remove Congo red from the blood stream.

Ten cubic centimetres of 1 per cent Congo red are injected intravenously and samples of blood are taken from the other arm at exactly five minutes and at one hour after the dye has been injected. The greatest care must be taken to avoid haemolysis. The proportion of dye remaining in the serum at the end of one hour is estimated by comparison with the five-minute specimen. *Congo red*

In the absence of amyloid disease more than 60 per cent of the original dye is usually still present in the serum after one hour, whereas in a patient with advanced amyloid, only a minute trace of dye may persist.

The urine for the same hourly period should also be sent to the laboratory, as excretion of dye in the urine, in some forms of renal disease, may, rarely, render the result doubtful.

(2) Bicarbonate

The normal range for serum or plasma bicarbonate is 55–75 volumes per cent of CO_2 bound as bicarbonate (23–33 m.-Eq. per litre). It is lowered in most conditions of acidosis, for example in renal disease and diabetes, and is raised in alkalosis. The relations of bicarbonate to other ions are discussed on page 86.

(3) Calcium

The calcium of the blood is wholly contained in the plasma, the corpuscles being calcium free. For this reason analyses for calcium are never made on whole blood.

(i) *Normal value.*—The calcium level in normal serum is one of the most constant findings, 9–11 milligrams per 100 cubic centimetres representing the normal range. Some of this calcium is bound to protein, and some free and ionized. The ionized calcium is the important fraction from the point of view of prevention of tetany, but unfortunately there is no direct way of measuring it for clinical purposes. In broad terms it may be said that a low serum calcium with normal serum protein (as in hypoparathyroidism) means a low ionized calcium and indicates a disturbance of calcium metabolism which is often associated with tetany, whereas a low serum calcium without tetany, associated with low serum protein (as in chronic nephritis) is probably only secondary to the condition causing the fall in protein. In a healthy subject serum calcium remains exceedingly constant throughout the day, and is practically uninfluenced by diet or even by the ingestion of calcium salts. *Ionized calciu*

Grossly excessive doses of vitamin D may raise serum calcium above normal.

Parathyroid dysfunction

(ii) *Serum calcium in disease.*—The *parathyroid hormone has very marked* action on the level of serum calcium. Hyperparathyroidism (adenoma) causes a high calcium level (12 milligrams or even up to 20 milligrams per 100 cubic centimetres), while hypoparathyroidism (idiopathic or post-operative) is associated with a low level (5–7 milligrams per 100 cubic centimetres). The high calcium in hyperparathyroidism is often associated with very low serum inorganic phosphorus (1–2·5 milligrams per 100 cubic centimetres). This is of diagnostic value, as the majority of other causes of multiple bone disease, *such as carcinomatosis, which may show high calcium values, have a normal* phosphorus level. In multiple myelomatosis a high calcium is sometimes found, and is often associated with a raised serum protein. In the diagnosis of

Tumour

parathyroid tumour a high calcium, low phosphorus and normal protein in the serum with a very high urinary excretion of calcium, are together very suggestive though unfortunately not always present. Multiple myelomatosis is sometimes very difficult to exclude as it may show very similar chemical changes.

Low serum calcium, apart from hypoparathyroidism, is associated with inadequate calcium absorption as in a few cases of rickets, osteomalacia, steatorrhoea, sprue and coeliac disease. If the serum calcium falls to between

Tetany

6 and 7 milligrams per 100 cubic centimetres, tetany frequently occurs. Low serum calcium is met with where plasma proteins are low, as in chronic nephritis, in malnutrition due to gastro-intestinal carcinomatosis and occasionally even in chronic sepsis. This form of hypocalcaemia is usually not associated with tetany.

(4) Chloride

On account of uneven distribution, chloride determination should always be made on serum or plasma, never on whole blood. The normal range is 345–370 milligrams per 100 cubic centimetres (as chlorine), 570–615 milligrams per 100 cubic centimetres (as sodium chloride), or 98–105 m.-Eq. per litre. The cells contain rather more than half as much chlorine as does the plasma. Serum chloride in relation to other ions is discussed on p. 86.

(5) *Cholesterol*

The normal range for blood cholesterol is 100–250 milligrams per 100 cubic centimetres for total cholesterol, rather more than half being free cholesterol and the remainder in the form of esters. Low blood cholesterol is found in many forms of anaemia and cachexia; raised blood cholesterol is found in nephritis (oedematous stage), diabetes, pregnancy and multiple xanthomatosis. Changes in cholesterol in liver disease are discussed on p. 83. The level of blood cholesterol forms roughly a mirror image of the basal metabolic

Control in treatment of thyrotoxicosis

rate, being low in thyrotoxicosis and high in myxoedema; a rise in the plasma cholesterol above normal during treatment with thiouracil is a warning of overdosage and an indication to withhold further treatment.

(6) Creatinine

The normal range for blood creatinine is 0·7–2 milligrams per 100 cubic centimetres. It is raised in chronic nephritis and urinary obstruction. On the whole, the rise, proportional to the rise in blood urea, is less in renal

obstruction than in chronic nephritis, but in individual cases the diagnosis between a high blood urea due to uraemia and one due to obstruction cannot be made by means of creatinine determinations.

(7) Diastase

Diastase is an enzyme which has the function of breaking down complex carbohydrates into simpler sugars. Diastase is excreted in the urine, and its determination is of value in the diagnosis of acute pancreatitis.

Wohlgemuth unit

Urinary diastase is usually expressed in Wohlgemuth units. One unit expresses the amount of diastase which will digest 1 milligram of soluble starch in 30 minutes at 37° C. There is some variation in the amount in normal urine, ranging from about 6–33 units per cubic centimetre, with occasional values as high as 50 units in very concentrated specimens.

Acute pancreatitis

The principal condition in which urinary diastase determinations are of value is acute pancreatitis. In this condition an enormous rise in urinary diastase may be found, up to more than 1,000 units per cubic centimetre. Any figure above 100 units may be regarded as confirming the diagnosis, and a value of 250 units or more makes the diagnosis practically certain.

After operation, the urinary diastase rapidly falls and is usually normal in a week or so. Without operation, if the patient survives, the fall takes place rather less rapidly.

In chronic pancreatic disease the estimation is of little value, normal figures being usually found. Very low values are often, but not invariably, found in cases of carcinoma of the pancreas.

Nephritis

In nephritis, very low diastase values are found, and in the presence of advanced renal disease a raised urinary diastase may not be found even in cases of acute pancreatitis. Very high figures for blood diastase (normally 3–10 Wohlgemuth units) may be regarded as confirming the diagnosis of acute pancreatitis, but in the presence of renal failure moderate rises are not of any significance. A rise in the blood diastase in mumps has been reported by some observers.

(8) Faecal fat

The fat in faeces occurs in three fractions: neutral fat, fatty acids and soaps. The neutral fat is fat which has not been hydrolysed by the pancreatic ferments and is often called "unsplit fat". The proportion of fatty acids to soaps depends merely upon the hydrogen ion concentration in the intestine and is of no significance. Fatty acids and soaps together are called "split fat".

Normal values

In normal faeces, the total fat should be not more than 25 per cent of dry weight of faeces, and the "unsplit fat" not more than 25 per cent of the total fat; very slightly higher figures may be found in children.

In pancreatic and liver diseases the total fat content may be much higher than normal, up to some 75 per cent of dry weight; typically in chronic pancreatitis high total fat with a high proportion of neutral fat is found, while in jaundice due to obstruction above the pancreatic duct, a high percentage of fat, the greater part of which is split, is found.

Intestinal malabsorption

Very high figures for faecal fat, usually well split, are found in conditions of intestinal malabsorption, such as sprue, some forms of idiopathic steatorrhoea and tuberculous blockage of the lacteals.

Recent work has shown that greater information can sometimes be obtained by placing the patient on a fixed fat intake (50 grammes *per diem*) and estimating the total fat output in the faeces over a period of 3–4 days. In a normal person some 95 per cent of the fat is absorbed, but in some cases of fat intolerance, lower absorption (say 75–80 per cent of intake) may be found, although the percentage content of fat in the faeces may be within normal limits.

(9) Phosphate

The phosphorus of blood occurs in many forms, but only the inorganic phosphate is of immediate clinical importance.

The normal inorganic phosphate usually ranges from 2·5–4 milligrams per 100 cubic centimetres, the value in children being rather higher—usually 4 to 6 milligrams per 100 cubic centimetres. Serum inorganic phosphate is inversely associated with the serum calcium, and generally a rise in phosphate is associated with a fall in calcium, and vice versa.

Low serum inorganic phosphate is found in rickets, osteomalacia and hyperparathyroidism. Raised serum inorganic phosphate is found in the late stages of chronic nephritis and in some cases of renal infantilism; it is sometimes found during the healing of a fracture, and in patients with multiple secondary deposits in bone. In idiopathic hypoparathyroidism raised serum inorganic phosphate is sometimes found, though in hypoparathyroidism after parathyroidectomy the level is usually within the normal range.

(10) Phosphatases

The phosphatases are enzymes which hydrolyse organic esters of phosphoric acid, liberating inorganic phosphate. In clinical medicine two types of serum phosphatase are distinguished: "alkaline phosphatase" which acts best at a very alkaline *p*H, and "acid phosphatase" which is most active about *p*H 5·0.

(i) *Serum alkaline phosphatase.*—This is usually expressed in King and Armstrong units, most normals falling between 5 and 10 units per 100 cubic centimetres, with an extreme normal range of 3–13 units. In American literature, Bodansky units are frequently used, the normal range being 1·5 to 4 units. Higher normal values for phosphatase are found in children.

Increased in bone diseases

This value is raised in many generalized diseases of bone, especially Paget's disease and rickets, in which values of over 50 units are frequently found. Raised values are also found in generalized osteitis fibrosa, and often in multiple secondary deposits in bone, but the values here are not usually so high, 20–40 units being more usual figures. In carcinoma of the prostate the alkaline phosphatase is frequently raised as well as the acid phosphatase. Apart from bone disease, alkaline phosphatase is markedly raised (30 units or more) in obstructive jaundice and sometimes in cirrhosis of the liver.

(ii) *Serum acid phosphatase.*—This has a normal range up to about 3 units per 100 cubic centimetres though, occasionally, normal individuals may have values as high as 5 units.

Prostatic carcinoma

In carcinoma of the prostate with bone metastases raised values are usually found, sometimes to very high figures. The highest value we have met with is 304 units; more commonly values of 10–30 units are found, and sometimes values are practically within the normal range. Although there is very little doubt that the prostate is the origin of the raised acid phosphatase found in prostatic carcinoma, the normal acid phosphatase

has a different, unknown, origin (it occurs in the serum from women), and in the border-line cases differentiation can sometimes be made through the observation that prostatic phosphatase is rapidly destroyed by the action of alcohol, whereas normal phosphatase is unchanged. For example, an acid phosphatase of 5 units which is reduced to 3 units after treatment with alcohol is probably associated with carcinoma of the prostate, whereas one of 5 units which shows insignificant change with alcohol is probably normal. In the absence of bone metastases, patients with prostatic carcinoma frequently give normal values, and the enzyme level is always normal in prostatic hypertrophy. The raised acid phosphatase in carcinoma is reduced by treatment with oestrogens, though it may take several weeks to return to normal; the alkaline phosphatase in these patients takes even longer to return to normal.

(11) Proteins

The proteins of plasma comprise three main fractions: fibrinogen, globulin and albumin. In clinical work estimations are frequently carried out on the serum, which of course contains only globulin and albumin. The plasma proteins can be further subdivided into a greater number of fractions, but this is not practicable in a clinical laboratory at present. The globulin comprises two main fractions $\alpha\beta$-globulin, and γ-globulin; most of the immune bodies of serum are associated with the γ-globulin.

Normal values

Normal values are 5·8–8 per cent for total plasma protein, which comprises 0·2–0·4 per cent fibrinogen, 1·5–3·0 per cent globulin and 3·5–5·5 per cent albumin.

In disease there may be a rise in plasma protein with normal proportions, through haemoconcentration, as in gross dehydration, due to cholera or other causes of severe diarrhoea or severe and acute vomiting, but usually the proportions of the various proteins are altered.

Very high serum protein, usually due to rise of globulin, with normal or low albumin, is met with in kala-azar and in multiple myelomatosis; figures such as 1·2 per cent of albumin and 11·5 per cent of globulin are met with in the latter. The rise in multiple myelomatosis is sometimes due to a rise in the $\alpha\beta$-globulin and sometimes in the γ-globulin. The rise cannot be shown to be due to Bence-Jones protein in the majority of cases, though sometimes its presence can be demonstrated.

Chronic nephritis

Low serum protein, usually with a disproportionately greater fall in albumin, occurs in many conditions. In nephritis, particularly in the chronic active stage, low protein—especially low albumin—is met with. There is a fairly close correlation between protein level and oedema: if the total protein is less than 5 per cent, or the albumin less than 2·5 per cent, oedema is usually present, and with protein values higher than these it is usually absent. In chronic malnutrition due either to prolonged inadequate protein intake or to chronic gastro-intestinal disease, there is also a low protein level. This is sometimes of surgical importance, as it may be impossible to rectify salt abnormalities in the blood unless the plasma protein is at the same time restored to normal by the administration of plasma. In many infections there is low albumin together with high globulin, the total protein usually being somewhat reduced.

The changes in serum protein in liver disease are discussed on p. 82.

(12) Sodium

The normal serum sodium range is 315–335 milligrams per 100 cubic centimetres or 137–144 m.-Eq. per litre. Changes in serum base, of which sodium forms the chief part, are discussed on p. 84.

(13) Uric acid

The normal blood uric acid content is 2–4 milligrams per 100 cubic centimetres. Uric acid determinations are usually made to confirm the diagnosis of gout, in which raised values of the order of 5–6 milligrams per 100 cubic centimetres are usually met with, though in some genuine cases of gout the rise is negligible. High values also occur in renal failure, eclampsia and leukaemia, and the rise in these conditions may be far greater than that met with in gout.

Causes of rise

9. COLLECTION OF SPECIMENS

(1) Blood

To take full advantage of biochemical analyses it is essential that blood should be taken under the proper conditions and handled properly prior to analysis. There is no value in having analytical methods accurate to say 1 per cent, if the previous handling of the blood leads to a variation of several per cent in a certain constituent. For this reason a general account is given of the proper methods of taking blood for various tests.

For many methods the blood is best obtained by finger prick, taken up into a calibrated capillary pipette and washed straight from it into an appropriate solution, but if blood is being sent a distance this is impracticable and venous blood is required. The following notes may be helpful in producing satisfactory blood samples.

(2) Choice of whole blood or serum or plasma

Certain blood constituents such as urea are evenly distributed between cells and serum, and for these it is immaterial which is used for analysis. In others, such as glucose, distribution is somewhat uneven, but custom and convenience have led to most determinations being made on whole blood. The distribution of sulphonamides between cells and corpuscles is grossly unequal and varies from one sulphonamide to another. Nevertheless, most of the previous work has been done on whole blood, and for convenience whole blood will continue to be used. The majority of determinations of the non-protein nitrogenous constituents are usually carried out on whole blood.

In contrast to the above, analyses of whole blood for any of the inorganic constituents are for ordinary purposes useless, as they are very unevenly distributed between cells and plasma.

(3) Anti-coagulants

Various substances are used to prevent blood clotting. The commonest are sodium oxalate, potassium oxalate, potassium fluoride (for blood sugar), sodium citrate, lithium oxalate and heparin.

For the prevention of clotting when analyses are to be made on whole blood, an oxalate (in reasonable quantity) is usually used. Fluoride is used when taking blood for sugar analysis, if analysis is not to be performed immediately,

as it prevents glycolysis which may proceed rapidly in warm weather in plain oxalated blood and may lead to low results. Fluoride blood cannot be used for urea determination by the urease method, as the fluoride is inhibitory to the enzyme.

Heparin is the most satisfactory all-round anti-coagulant, but is not widely used on account of expense and the difficulties of supply. Owing to the osmotic changes produced by the other anti-coagulants, heparin is the only one reasonably satisfactory for use when any of the electrolytes are to be determined, but, for simplicity, serum is usually used for all determinations of inorganic constituents.

(4) Avoidance of haemolysis

Haemolysis interferes with many tests, not only biochemical, and must be avoided. The following points will aid in avoiding haemolysis. The syringe is preferably dry-sterilized; an all-glass syringe is desirable and may be lubricated with liquid paraffin. If for any reason a wet syringe has to be employed, it must be rinsed out thoroughly with normal saline, and not with water; ether should not be used for drying, as traces very easily produce haemolysis. The blood should be delivered into the container slowly, after the needle has been removed; forcible squirting through the needle causes gross haemolysis.

(5) Determination of inorganic constituents

For accurate estimation of sodium, chlorine and bicarbonate, loss of carbon dioxide from the blood should be avoided. If CO_2 escapes, water and chlorine ions pass from cells to plasma, and the composition of the serum when separated differs from that which it had in the circulation. For accurate work "true" serum can be obtained without difficulty by the following technique.

About one inch of liquid paraffin is placed in a small screw-capped bottle (universal container). Liquid paraffin is also placed in a well-fitting syringe so as to eliminate all dead-space in the nozzle and needle. The arm is compressed by a nurse to make the veins prominent, the needle is inserted and the blood withdrawn. Pressure must not be applied for more than a few seconds before the needle is inserted, and a tourniquet should not be used, as stasis causes changes in the CO_2-content of the blood. After the blood has been obtained the point of the needle is passed below the liquid paraffin in the container, and the blood gently and slowly expelled under the paraffin layer. The bottle is then filled right to the top with paraffin and the screw-cap replaced. It is useless merely to cover the blood with a layer of paraffin in an open tube; CO_2 rapidly diffuses through the paraffin and is lost.

If blood is taken without these precautions, errors in the sodium, chlorine and bicarbonate levels occur and it is necessary to appreciate their magnitude. The sodium and chlorine levels are usually not more than 4 per cent low, but the bicarbonate may be low by as much as 10 per cent. Figures with this degree of inaccuracy may be sufficient to diagnose a severe acidosis, but are undesirable in accurate scientific work.

For calcium, potassium and phosphate determinations these precautions are not necessary, but it is essential to separate the serum within 2–3 hours at most for estimation of potassium and inorganic phosphate. If serum is left in contact with clot for longer than this, potassium begins to diffuse out and serum obtained after standing overnight in contact with clot may have a potassium content 100 per cent higher that it had originally; the cells also contain large quantities of organic phosphoric esters, and these gradually break down on standing to produce erroneously high values for inorganic

phosphate. Scrupulous avoidance of haemolysis is essential in all work on serum potassium. The way in which blood should be taken for the various tests is shown in the Table.

10. BLOOD SPECIMENS REQUIRED FOR VARIOUS TESTS

For the majority of tests, about 10 cubic centimetres of blood should be sent to the laboratory. Although some tests can be carried out on smaller quantities, laboratory examination is facilitated and doubtful results can be more readily checked if material is plentiful. If several tests are required on the same specimen, e.g. calcium, phosphate and phosphatase, 20 cubic centimetres should be sent. Blood and other specimens are much more conveniently taken in small bottles with screw-caps than in test tubes.

The form in which blood is required for various tests is shown below.

TABLE SHOWING FORM OF COLLECTION OF BLOOD FOR VARIOUS TESTS

Alkali reserve	Preferably D; less satisfactory A or B	Liver function (colloidal tests)	A
Amyloid (test for)	A	Phosphate	A or B
Bile pigment (van den Bergh or icterus index)	A or B	Phosphatase	A or B
		Protein	Usually A
Calcium	A	Sodium	Preferably D; alternatively A
Chloride	Preferably D; less satisfactory A or B	Sugar	C
Cholesterol	A or B	Sulphonamides	B
Creatinine	B	Urea	B
Diastase	B	Uric acid	B (Lithium oxalate is preferable to potassium oxalate)

A = blood taken in sterile container without anti-coagulant.
B = blood taken in container with potassium oxalate.
C = blood taken in container with fluoride.
D = blood taken in container, under paraffin, to avoid loss of carbon dioxide.

11. URINE SPECIMENS

All specimens of urine for biochemical tests must be obtained cleanly and as fresh as possible; in a few hours bacterial activity can alter materially the composition of urine. If immediate analysis is impossible a few drops of toluene or a crystal of thymol should be added, and the specimen kept as cold as possible.

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[References to other titles are given under Biochemical Tests—Curves and Charts in the Index Volume. The subject of Blood Examination is also dealt with in the *British Encyclopaedia of Medical Practice* (1936), Vol. 2, p. 457.]

BITES AND STINGS

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1. MAMMALIAN BITES

53.] Domestic animals are responsible for most of these injuries. Human beings may also be concerned and bites from children and lunatics are not uncommon. Bacteria abound in the mouth, and the presence of decayed organic matter provides an ideal medium for the transference of infection. Attacks by the larger hunting animals are associated with violence which, apart from injuries by teeth and claws, may result in mangled limbs, internal injuries and avulsion of tissues. These cases are usually remote from surgical aid, and the victims are subjected to long and painful carriage while suffering from exhaustion, haemorrhage, dehydration and psychical shock. Jungle warfare has taught that transport by water or even hand-litter, though slower, may be preferable to a rough transportation by vehicle. *Hunting animals*

The treatment of compound injuries in no way departs from standard surgical principles. The wounds are always grossly contaminated and treatment is often delayed. Resuscitation, blood transfusion, plasma transfusion and restitution of fluid loss necessarily precede the full exploration and thorough surgical toilet which the case demands. Anti-gas-gangrene and anti-tetanic sera should be given in all cases and penicillin and sulphonamides if available, but none of these should obscure the necessity for full surgical intervention. *Treatment*

Bleeding should be provoked in small punctured wounds, if seen early, and the wounds washed and cauterized. Larger wounds should be treated as for any laceration. Bites from rabid animals should be left unsutured and all suspected cases removed to a Pasteur Treatment Centre. *Punctured wounds* *Rabies*

Many adverse conditions exist in the tropics. Exposed wounds are often invaded by insects and larval deposits. Maggots are harmless, but no patient *Wounds in tropics*

will tolerate them in the nostrils and face. Screw and mosquito worms, mainly found in Central America, not only infest wounds but may penetrate accessory sinuses and natural orifices. Fresh blood attracts mosquitoes. Malaria and dysentery are frequent intercurrent complications. Ureteric colic and urinary suppression must be remembered during the administration of sulphonamides, and regard paid to fluid intake and output. Dietary and vitamin deficiencies are encountered. Plaster casts are preferable to bulky dressings; adhesives are ill tolerated. Patients with suppurating wounds may be saved much misery from flies by nursing under a net.

2. SNAKE BITE

(1) Definition

Venom is a poisonous secretion which, injected into the tissues, produces effects which may be predominantly neurotoxic or haemolytic.

(2) Species

Of the 1,700 varieties of snakes described, some 300 of the Colubridae and Viperidae are poisonous to man. Every surgeon should become familiar with the species and habits of snakes to be found in his district, for correct treatment is dependent upon accurate identification. Non-poisonous snakes, for example those not possessing specialized fangs, may secrete a poisonous saliva, capable of causing an intense inflammation. The fangs of the Colubrines are grooved anteriorly and the maxillae relatively fixed. The maxillae of the vipers are capable of vertical rotation; the fangs are more developed and canalized. Vipers are not difficult to identify, with their broad, triangular, flattened heads, constricted necks, thick bodies and squat tails. Sea snakes are all poisonous, but recorded bites are few. Freshwater snakes are harmless.

Identification

(3) Method of biting

Vipers strike hard, bite and retreat. Colubrines often hang on, and their removal may be difficult. Full biting force and discharge of venom are exercised only when the lower jaw is fixed, which fact accounts for the superficial wounds when the snake strikes obliquely. Colubrine fangs are so grooved that some of the venom may be spilled, in contrast to the canalized teeth of the viper, which bite and inject deeply and forcibly into the tissues. At least 50 per cent of all bites occur below the knee.

(4) Clinical picture

Effects become apparent within a few minutes or are delayed for some hours. In all cases the cardiovascular system suffers early, with prostration, faintness and vomiting.

(*a*) *Colubrine*

Locally there is burning, stinging pain in the bitten area, followed by rapid swelling. Quite early there is muscle weakness, inco-ordination and visual disturbance. Salivation may be profuse, with inability to swallow. Breathing is rapid, but soon becomes shallow and laboured. Asphyxia and convulsions precede complete respiratory failure.

(*b*) *Viperine*

As before, there is burning, persistent pain. Punctures are not always visible, particularly with certain tree snakes. A thin, continuous, blood-stained

discharge is usual. Discoloration and local extravasation are rapid, as are collapse and the onset of vomiting. Bleeding from the gums and nostrils, a blood-stained vomit, haematuria and effusion into serous spaces may all be evident.

The later picture is that of wide local necrosis, sepsis, vascular impairment and gangrene. A temporary improvement may be observed, only to terminate fatally in the succeeding days as the result of suppuration, toxaemia, exhaustion and cardiovascular failure.

(5) Differential diagnosis

Diagnosis is usually evident. The snake should be killed and identified as poisonous or non-poisonous, colubrine or viperine. Bites from small rodents and scorpions should be remembered. *Poisonous or non-poisonou*

These signs are helpful in decision :

(a) pain—when persistent and severe ; (b) discoloration, oedema and local extravasation; (c) persistent blood-stained discharge.

Terror may produce a state of utter collapse. The case of a woman found in such a condition is related. She was alleged to have been bitten in the buttock in an outdoor latrine. Two small punctures were visible. A search for the snake revealed an imprisoned hen ! *Terror*

Ataxia, perhaps with disturbance of speech and vision, may resemble alcoholism.

(6) Treatment

(a) Application of an effective ligature to delay the absorption of venom.
(b) Removal of venom by local means.
(c) Specific antivenene.
(d) Treatment of complications as they arise.

The ligature must be applied immediately and tightly enough to obstruct the circulation. Application is made over a protective covering—in the leg above the knee, in the arm above the elbow. The limb, in the dependent position, may be exsanguinated from the ligature towards the lesion by pressure with the hands or a tight bandage. The wound and surrounding skin are washed to remove spilled venom. If the bite is on the face, neck or trunk, an attempt at localization may be made by pressing hard over the wound with the rim of a cup or any similar article available. *The ligature*

Excision should be attempted after application of the ligature. For this purpose some make a habit of carrying a sealed safety-razor blade, preferably one with a single edge, which is safer for the operator. A quick incision between and at right angles to the fang marks, followed by elliptical cuts joining the sides of the first and including the punctures, removes much of the venom, leaves the wound widely open, and can be made in a few seconds. Sucking should be resorted to only when excision cannot be performed, and then only with shielded lips. After excision the wound should be washed with a solution of potassium permanganate, and the ligature loosened to allow this part to be flushed with blood, but still sufficiently tight to obstruct the venous return. It should not be retained continuously for more than twenty minutes after the first application, and thereafter at shorter intervals up to a period of from 2 to 2½ hours. *Excision* *Managemen of ligature*

In situations in which a ligature cannot be applied, treatment is limited to washing, localization, excision and mechanical suction.

Carriage The patient should be carried with the part immobilized, and be accompanied by someone capable of manipulating a ligature properly.

Antivenene Antivenenes are available against the vipers and colubrines of West and South Africa, cobras, and Indian, Brazilian, North American, European and English vipers. Antivenene must be injected with the least delay. Ampoules usually contain 20 cubic centimetres; 10 cubic centimetres are generally sufficient. In severe cases the full 20 cubic centimetres should be given intravenously and slowly.

Spat venom Spat venom of cobras is without danger except when directed into the eye or a breach of the skin. The eye should be bathed and antivenene, diluted with saline, instilled. Pain is rapidly relieved.

(7) General management

The patient should be kept warm and the part immobilized; watch is kept for excessive salivation and laryngeal paralysis.

Coramine is a safer stimulant than strychnine. Artificial respiration should be begun early in the event of threatened respiratory failure. Pituitary extract or adrenaline may be given for circulatory failure. Calcium chloride in doses of 15 grains is said to be of value in viper bites. At a later stage suppuration, tetanus and gangrene may demand appropriate intervention.

(8) Conclusion

Where snakes are common, antivenene, a syringe, rubber tubing and a good electric torch should be readily available, always in the same place and used for no other purpose. Assistants should be instructed exactly how to proceed if alone. A wall chart illustrating common snakes is helpful. Finally, it is a duty, not merely for one's own security but also to the community which one serves, to cultivate in the tropics an awareness of danger and possible attack, an attribute which modern civilization does little to foster.

3. POISONOUS FISH

Bites by poisonous fish are common in tropical waters. Apart from the ability to inflict savage and mutilating bites, many fish are provided with specialized teeth, poison glands and poisonous barbed fins.

Sting-ray The sting-ray attacks by swimming backwards and spearing its victim with a thrust of the tail. The caudal spine is frequently broken off and left embedded in the wound, generally in the foot. These wounds are characterized by intense pain, which morphine does little to relieve. The spine is usually demonstrated by a skiagram and must be removed. A few poisonous fish inhabit British waters; these are the weevers, sting-rays and spiny dogfish. The sting is acutely painful, but inflammation is usually local and short-lived.

Bites by poisonous fish may result in profound shock and collapse. Respiratory or cardiac failure and rapid death are not uncommon.

Treatment Treatment is directed to the removal of venom locally and to combating the effects of that already absorbed. Local infiltration with 2 per cent procaine hydrochloride may relieve, but pain may be so severe and persistent that narcosis by infusion with Pentothal (Thiopentonum Solubile, *B.P.*; Pentobarbital Sodium, *U.S.P.* XII) in normal saline may have to be employed.

4. SCORPIONS

Venom is stored in paired glands in the post-anal segment of the tail. When attacking, the tail is flicked forwards, held to the skin by a terminal barb and by the anterior appendages. Ejection of venom causes immediate intense pain. Effects are usually local but alarming general manifestations may follow. Oedema may be marked, especially in the genitalia, a not uncommon site of attack. The condition usually subsides within three hours. Liquor Ammoniae Fortis, if applied at once, may relieve pain, but more certain relief is obtained by a subcutaneous injection of procaine hydrochloride solution. *Treatment*

Fatalities occur in children, for whom some advise ligature, incision and irrigation as for snake bite.

An efficient specific antivenene can be used. Sergent (1943) suggests first that the injection of normal saline may prevent death in the experimental animal, and secondly that saline can be given advantageously with antivenene. *Specific antivenene*

5. SPIDERS

The majority of the Araneae are equipped with poison glands, but for the most part the venom is harmful only to their natural prey. Inflammatory reactions are often due to organic matter present about the mouth. Haemolysins and neurotoxins are contained in the venom and, in addition to local inflammation and paresis, the general effects may include respiratory distress and cardiovascular failure. *Venom*

The tarantula is found only in Southern Europe, and is often confused with the large bird-eating species of Central Africa and elsewhere. Neither is particularly dangerous. *Habitat*

The usual *consequence of a bite is the rapid onset of inflammation, cellulitis* and lymphangitis. The area becomes swollen and numb or the site of irritation. Gangrene of the skin is not infrequent, but the slow, painful formation and separation of deep sloughs is more usual.

Treatment is that of acute inflammation. Anti-sera have been produced in certain localities and their use found beneficial. Healing, especially in the tropics, may be slow, and chronic ulcerative conditions are not infrequent.

6. CENTIPEDES

Centipede bites resemble those of spiders. The condition is painful, with local inflammation and lymphangitis. Sometimes wide areas of skin are raised into a superficial blister, similar to a second-degree burn. The blister should be trimmed with scissors and methylene blue or triple dye applied.

7. INSECTS

Insect bites may cause local inflammation, suppuration and septicaemia. The mobility of the face, with the absence of fascial barriers, makes it especially liable to such infections. Bites in the region of the upper lip, nose and orbit are among the causes of cavernous sinus thrombosis. In such infections rigid non-interference is indicated, particularly from the patient and the inquisitive fingers of attendants. Ligature of the angular vein is an uncertain method of *Danger area of face*

checking the spread of infection and is not without danger. Penicillin or sulphonamides, given early, with the exercise of general measures, is suggested as the treatment of choice.

Anaphylaxis Anaphylaxis may occur in persons sensitized to the stings of wasps, bees and hornets. The stings should be removed without compressing the poison sac. For relief of pain, ammonia is suitable for bee stings and dilute acetic acid for hornets and wasps.

The irritation caused by ants, midges and mosquitoes may be treated by the application of carbolic lotion, and small vesicles and sores with methylene blue.

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[References to other titles are given under Bites and Stings in the Index Volume. The subject of Bites and Stings is also dealt with in the *British Encyclopaedia of Medical Practice* (1936), Vol. 2, p. 343.]

BLACKWATER FEVER

See SURGERY IN THE TROPICS

BLADDER—INFECTIONS

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1. DEFINITION

54.] Simple cystitis, as a clinical entity, is a rare condition. Bacteriuria and pyuria commonly occur without inflammatory changes in the wall of the bladder. The undamaged vesical mucosa has a high resistance to organismal invasion, and the special properties of the living transitional epithelium render toxic absorption very slight, when the bladder wall is healthy and there is no obstruction to emptying. The bladder wall has a complete sensory innervation through the afferent fibres of the parasympathetic nerves from the second, third and fourth sacral segments of the spinal cord (Learmonth, 1931a). During cystoscopy the patient can be made aware of sensation of heat and cold, or touch and pain, produced by the endoscopic manipulations and

Sensory innervation of bladder

Inflammation and dysfunction

treatment. Inflammations of the bladder wall leading to disturbance of function and irritation of the nerve endings bring about the clinical picture of cystitis, accompanied by increased frequency, urgency and dysuria. Although the bladder is seldom primarily invaded by organismal infection, its anatomical relations to the upper and lower urinary tracts and the genital organs and ducts render it specially prone to secondary invasion by direct extension of an infective process from one or the other. Thus it would be more definitive in diagnosis to term descending urinary tract infections cases of pyelocystitis, omitting for simplicity any reference to foci of infection in the renal parenchyma. Similarly, ascending infections limited to the bladder might be referred to as cases of urethro-cystitis, again omitting the primary source from the prostate or seminal vesicle.

2. AETIOLOGY

Factors accessory to infection

Obstruction, trauma and a lowered general resistance are three factors which render the bladder more prone to infection, even though the route of invasion may be from the upper urinary tract, the genital organs, direct implantation, or the blood stream.

(1) Obstruction

Vesical obstructions form the most important of accessory factors leading to infection. Such obstructions may be congenital or acquired. (*See* Table.)

CAUSES OF VESICAL OBSTRUCTION

Congenital	*Acquired*
Congenital phimosis	Acquired phimosis
Atresia	Stricture
Posterior urethral valves	Urethral calculus
Hypertrophied verumontanum	Prostatic obstructions
Contracture of the bladder neck	Vesical calculus
Achalasia of the bladder neck	Vesical diverticulum
Abnormal openings and anomalies	Vesical tumour

(2) Trauma

Nature of trauma

The bladder wall may be injured by the presence of a calculus, or of foreign bodies introduced by accident or design. Missiles, penetration by fragments from fractures of the pelvic bones, sequestra from osteomyelitis of the pelvis, foreign bodies introduced *per urethram*, indwelling catheters, the presence of non-absorbable sutures and the like, all produce a local irritation of the vesical mucosa. Such lowering of the resistance of the tissues locally as a result of trauma may be seen when over-energetic local therapy by chemical antiseptics leads to necrosis of the bladder mucosa.

(3) Lowered general resistance

General debility from intercurrent disease, avitaminosis and faulty personal hygiene, all contribute to a general lowering of the resistance to infection. The periodicity of attacks of cystitis in women, who suffer from a persistent bacteriuria, may be observed in relation to alterations in the health and habits of the individuals concerned.

3. MODE OF INVASION

(1) Intraluminar

The intraluminar extension of infections to the bladder from the upper or lower urinary tracts is commonly seen when cystitis is associated with pyelonephritis or posterior urethritis. The bacteria invading from the upper and lower urinary tracts multiply rapidly in the urine which accumulates in the bladder between acts of voiding. Whereas the primary foci of infection in the urogenital tract may be from a haematogenous source, e.g. the renal parenchyma or the prostate and seminal vesicle, the route of extension to the bladder is by the infected urine or the infected secretions of the prostate and seminal vesicle in their respective channels. In the female, infections may extend to the bladder from the short wide urethra (Hanley, 1946). *Spread of infection in urinary tract*

Implantation of infection by the catheter is a source of infection which is very common and of great importance, especially when the passage of the catheter leads to trauma and the resistance of the bladder has been lowered by the presence of residual urine.

(2) Extension from adjacent organs

Occasionally there may be a direct extension of infection to the bladder from a neighbouring organ. For example, in appendicitis or diverticulitis with abscess formation, there may be an associated cystitis, which may lead to confusion in diagnosis unless a complete examination is made. Rupture of the abscess may lead to persistent vesico-intestinal fistula. The common *Bacillus coli* infections of the urinary tract are usually regarded as blood-borne infections with primary foci in the renal parenchyma or the accessory genital organs. The route of spread from the bowel to the blood stream is not fully understood. It has become accepted that the organisms gain entry to lymphatic channels, and pass thence to the intermediate and central glands, and thence again into the circulation. *Spread by contiguity* *Indirect infection*

(3) Lymphogenous

The venous plexus of the bladder and the intercommunications between it and the venous return from all organs of the pelvis bring an accompanying network of lymphatic channels into close relationship. Thus a retrograde extension of infection to the bladder may occur via the lymphatics from the cellular tissue of the pelvis. This mode of spread may be seen in the more indolent and chronic forms of erosion of the cervix uteri, and prostatitis and seminal vesiculitis, when there is a persistent venous congestion of the organs concerned. *Retrograde lymphatic spread*

(4) Haematogenous

Although the urine from a case of localized interstitial cystitis of the bladder roof (Hunner's ulcer) contains no pus cells or bacteria, sections of the affected area of the bladder wall show a marked degree of inflammatory change in the submucous layer. The aetiology of this condition is unknown. It is customary to eradicate focal sepsis as a preliminary to local therapy, in the belief that some organism with an affinity for the bladder wall has reached this site via the blood stream. The persistence of a localized area of cystitis at this most mobile part of the bladder vault may be due to that most elementary factor in delayed healing, namely, absence of rest. *Relation of mobility of bladder vault to Hunner's ulcer*

4. BACTERIOLOGY

Organisms found in acid and alkaline urine

The organisms responsible for vesical infections may be divided into two major groups: (a) those found in an acid urine which include the *B. coli* group, *B. pyocyaneus*, *B. typhosus*, (b) those found in an alkaline urine which include streptococci, staphylococci, *B. proteus*. The presence of pus cells without organisms is an indication for repeated examinations for tubercle bacilli or the gonococcus. The *B. coli* group forms the commonest causal organism—especially so in women. The control of most coccal organisms by penicillin, and of certain coliform strains by the sulphonamide drugs, has led recently to a more frequent appearance of *B. proteus* and *B. pyocyaneus* in infections of the lower urinary tract. Recent developments in the chemotherapy of the organismal invaders of the urinary passages have not yet provided the ideal bactericidal agent, by whatever route of administration.

5. *MORBID ANATOMY AND CYSTOSCOPIC FEATURES*

(1) Acute infections

(a) Catarrhal cystitis
(b) Haemorrhagic cystitis
(c) Ulcerative cystitis

(*a*) *Catarrhal cystitis*

Dilatation of vessels

The vessels dilate and the mucosa loses its lustre. There are flame-like blushes of acute congestion and a flocculent deposit of purulent lymph. It is a characteristic feature that the illumination necessary for a cystoscopic inspection has to be considerably increased.

(*b*) *Haemorrhagic cystitis*

Haemorrhage and oedema

In this most acute form the bladder is intensely irritable and the capacity is greatly reduced. Blood wells up from the distended capillaries and the field of vision is reduced to a minimum unless continuous irrigation is maintained.

PLATE I(*a*).—Acute cystitis. Hyperaemia, oval ulcer and catarrhal debris.

(*b*).—Bullous oedema resembles a sessile papilloma, but the vesical mucosa is intensely congested.

(*c*).—Cystitis cystica. The minute cysts are translucent and are surrounded by a linear ring of congestion. Their well-defined nature is best seen in profile at the bladder neck.

(*d*).—Pseudo-membranous cystitis occurs on the trigone and consists of a pink apron of semi-organized catarrhal debris with some epithelial proliferation.

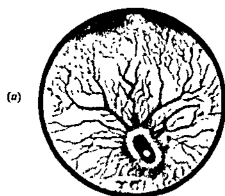
(*e*).—Membranous cystitis. A portion of slough has become organized. Incorporated with necrotic epithelium the cellular debris and amorphous phosphates form a tough membrane which is slow to separate.

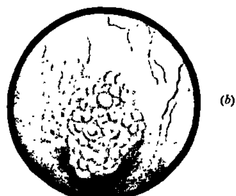
(*f*).—Incrusted cystitis. When a considerable phosphatic deposit occurs on a portion of slough or adherent and inspissated pus, the crystals accumulate and form an arborescence which closely resembles a necrotic papilliferous tumour.

(*g*).—Interstitial cystitis. Three patches of localized interstitial cystitis are shown. The chronicity is obvious from the scarring. The quiescent white scar, the active lesion with submucous congestion and the fissured ulcer which bleeds on distension of the bladder, are illustrated.

(*h*).—Tuberculosis. The small greyish-yellow tubercles are shown close to the retracted and slightly irregular "golf-hole" ureteric orifice. Confluence of the tubercles leads to an irregular shaggy ulcer.

(a)

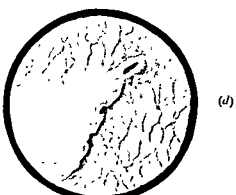




(b)

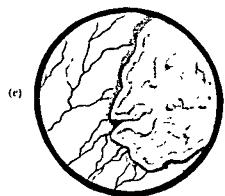
(c)

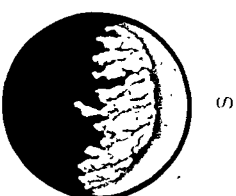




(d)

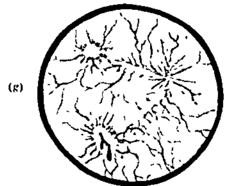
(e)

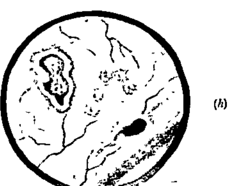




(f)

(g)





(h)

PLATE I

4. BACTERIOLOGY

Organisms found in acid and alkaline urine

The organisms responsible for vesical infections may be divided into two major groups: (a) those found in an acid urine which include the *B. coli* group, *B. pyocyaneus, B. typhosus,* (b) those found in an alkaline urine which include streptococci, staphylococci, *B. proteus.* The presence of pus cells without organisms is an indication for repeated examinations for tubercle bacilli or the gonococcus. The *B. coli* group forms the commonest causal organism—especially so in women. The control of most coccal organisms by penicillin, and of certain coliform strains by the sulphonamide drugs, has led recently to a more frequent appearance of *B. proteus* and *B. pyocyaneus* in infections of the lower urinary tract. Recent developments in the chemotherapy of the organismal invaders of the urinary passages have not yet provided the ideal bactericidal agent, by whatever route of administration.

5. MORBID ANATOMY AND CYSTOSCOPIC FEATURES

(1) Acute infections

(a) Catarrhal cystitis
(b) Haemorrhagic cystitis
(c) Ulcerative cystitis

(a) Catarrhal cystitis

Dilatation of vessels

The vessels dilate and the mucosa loses its lustre. There are flame-like blushes of acute congestion and a flocculent deposit of purulent lymph. It is a characteristic feature that the illumination necessary for a cystoscopic inspection has to be considerably increased.

(b) Haemorrhagic cystitis

Haemorrhage and oedema

In this most acute form the bladder is intensely irritable and the capacity is greatly reduced. Blood wells up from the distended capillaries and the field of vision is reduced to a minimum unless continuous irrigation is maintained.

PLATE I(*a*).—*Acute cystitis. Hyperaemia, oval ulcer and catarrhal debris.*

(*b*).—Bullous oedema resembles a sessile papilloma, but the vesical mucosa is intensely congested.

(*c*).—Cystitis cystica. The minute cysts are translucent and are surrounded by a linear ring of congestion. Their well-defined nature is best seen in profile at the bladder neck.

(*d*).—Pseudo-membranous cystitis occurs on the trigone and consists of a pink apron of semi-organized catarrhal debris with some epithelial proliferation.

(*e*).—Membranous cystitis. A portion of slough has become organized. Incorporated with necrotic epithelium the cellular debris and amorphous phosphates form a tough membrane which is slow to separate.

(*f*).—Incrusted cystitis. When a considerable phosphatic deposit occurs on a portion of slough or adherent and inspissated pus, the crystals accumulate and form an arborescence which closely resembles a necrotic papilliferous tumour.

(*g*).—Interstitial cystitis. Three patches of localized interstitial cystitis are shown. The chronicity is obvious from the scarring. The quiescent white scar, the active lesion with submucous congestion and the fissured ulcer which bleeds on distension of the bladder, are illustrated.

(*h*).—Tuberculosis. The small greyish-yellow tubercles are shown close to the retracted and slightly irregular "golf-hole" ureteric orifice. Confluence of the tubercles leads to an irregular shaggy ulcer.

The mucosa is markedly oedematous, and the areas of oedema may appear like sessile papillomas, resembling, as they do, bunches of dark purple grapes.

(*c*) *Ulcerative cystitis*

As the infective process persists, small groups of ulcers appear. These are circular or oval in shape and shallow in depth. The margins of the ulcer are clearly cut and not undermined. The base is darkly haemorrhagic, and bleeds readily as the bladder wall is stretched by the irrigating fluid. The ulcers may be solitary or in groups. This patchy distribution of the ulcerative lesions in acute cystitis is more characteristic towards the base of the bladder. (*See* Plate I(*a*).) ***Shallow ulcers***

(2) Chronic infections

(a) Lympho-glandular
(b) Cystitis cystica
(c) Pseudo-membranous cystitis
(d) Incrusted cystitis
(e) Leucoplakia
(f) Interstitial cystitis
(g) Pericystitis

(*a*) *Lympho-glandular*

A persistent cystitis leads to pericystitis as well as to more marked changes in the vesical mucosa under the influences of inflammation and repair. The bladder capacity has become diminished and the bladder wall more thickened. The mucosa shows a patchy variation from the normal straw-pink colouring to a dull red where the mucous membrane has lost its sheen. At the trigone the stimulus of chronic infection has led to a chronic oedema with swelling of the areolar tissue and bullous oedema. Sometimes at the bladder neck numerous glands undergo hyperplasia, so that the trigone becomes rough-surfaced like a cobbled roadway as opposed to the normal appearance of a flat pavement. (*See* Plate I(*b*).) ***Bullous oedema*** ***Glandular hyperplasia***

(*b*) *Cystitis cystica*

In this condition multiple small cysts are found on the trigone and bladder-neck areas. The cysts are translucent and surrounded by a linear congestion which is very characteristic. In profile the cysts are seen to be discrete and superficial. They are due to a hyperplasia of the transitional epithelium as a result of chronic irritation. The clear fluid within the cyst resembles colloid rather than mucus. (*See* Plate I(*e*).)

(*c*) *Pseudo-membranous cystitis*

This is one of the commonest manifestations of a chronic cystitis in the female. A greyish-pink false membrane forms from the base of the trigone to the bladder neck. It is a lesion which frequently accompanies urethritis or cervicitis. The membrane is false and consists of semi-organized inflammatory debris, at that most fixed portion of the bladder mucosa—the bladder trigone. (*See* Plate I(*c*).)

(*d*) *Incrusted cystitis*

A membranous cystitis following the organization of sloughing portions of the mucosa forms a ready nidus for the growth of bacteria. (*See* Plate

coincidence of the disease in the two systems, urinary and genital, is significant (Band, 1942). Nevertheless, tubercle of the bladder is usually secondary to renal tuberculosis. The earliest lesions are by intraluminar implantation from the ureter to the bladder. Greyish-yellow tubercles appear in the region of the ureteric orifice and the trigone. These ulcerate, become confluent, and form the characteristic greyish-yellow tuberculous ulcer, with its ragged undermined edges and zone of surrounding congestion. The ureter, discharging, as it does, tuberculous urine to the bladder, becomes itself involved in the tuberculous process. Tubercles develop in its walls, and the resultant fibrosis leads to a retraction and contraction of the ureteric tube, so that the ureter becomes foreshortened. This leads to the characteristic indrawing of the ureteric orifice, which becomes gaping, more widely dilated, and indrawn—the so-called "golf-hole" ureter. Its margins are often congested, ulcerated and irregular. (*See* Plate I(*h*).) The surrounding zone may show the presence of greyish-white or yellow tubercles. The bladder capacity is much reduced. The limitation of the disease to the neighbourhood of a ureteric orifice with characteristic changes is diagnostic. Confirmation may be delayed until the bacteriological diagnosis is made certain by guinea-pig inoculations, or cultural methods have confirmed the presence of the tubercle bacillus. In the male the possibility of bladder involvement secondary to genital tuberculosis has to be kept in mind in 10–15 per cent of cases (Moore, 1937).

Coincidence of renal and genital lesions

The tuberculous ulcer

"Golf-hole" ureter

Confirmation by cultural methods

(*b*) *Bilharziasis*

This disease has gained in importance as a result of two World Wars waged in Egypt and the African Continent. *Bilharzia haematobia* reaches the vesical veins by retrograde migration from the portal and mesenteric veins. The ova deposited close to the vesical mucosa work through to the bladder surface, where they appear as tubercles closely similar to those of *B. tuberculosis*. They are, however, larger than the tubercles of *B. tuberculosis* and, in colour, they are grey rather than yellow. There is a marked tendency to calcification, which may be recognized cystoscopically as sandy patches. Secondary infection is so common that proliferous granulations may form which closely resemble true papillomas with ulceration. The clinical history of terminal haematuria and strangury, the cystoscopic appearances, and the finding of ova, with their terminal spikes in the urine, confirm the diagnosis. It has been shown that the treatment of bilharziasis is entirely medical, using tartar emetic in a planned course amounting to a total dosage of 30 grains (Newman, 1943; Ward, 1945; Kirkaldy-Willis, 1946).

Similarity to tuberculosis

Similarity to papilliferous tumours

The treatment is medical

6. THE CLINICAL PICTURE OF CYSTITIS

Increased frequency, urgency and dysuria are symptoms which may be recognized in fully 90 per cent of cases of cystitis. Haematuria and pain may be present to a marked degree in 40 per cent. Pyuria is a constant finding. In urinary infections it is a characteristic feature to find the frequency constantly increased both by day and night. This contrasts with the frequency of micturition associated with emotional disturbance. Pain may be suprapubic, at the root of the penis (referred from the bladder neck), or in the perineum. It may be most pronounced at the beginning or end of micturition. In the former case the lesions are usually towards the vault of the bladder; in the latter they are

Symptomatology

Site of pain

Presence of urea-splitting organisms

I(*d*).) The pyogenic cocci and *B. proteus* are urea-splitting organisms and flourish in an alkaline medium. Triple phosphates are deposited as an amorphous mass on organic nuclei of slough, and, by accumulation, form arborescent incrustations which may resemble papilliferous tumours. (*See* Plate I(*f*).)

(*e*) *Leucoplakia*

An epithelial metaplasia

This rare condition may occur as plaques on the bladder base. The plaques are greyish white and are due to a cornification of the transitional epithelium, and a metaplasia to the squamous form. The aetiology of the condition is obscure; it resembles in many ways leucoplakia of the tongue, and is believed to arise from chronic irritation or from infection, stone, or, for example, the permanent indwelling suprapubic catheter. The epithelial metaplasia may be the precursor to cancer (Kretchmer, 1920).

(*f*) *Interstitial cystitis* (*Hunners' ulcer*)

The lesions appear at the roof of the bladder as star-shaped areas of intense congestion, which rapidly fissure as the bladder distends, and lead to bleeding (Hunner, 1930). This condition usually occurs in females. The bladder capacity is reduced, and in long-standing cases the wall is considerably thickened.

Aetiology obscure

The aetiology is obscure. It has been suggested that the lesion is a submucous inflammation due to blood-borne infection from a distant focus. The urine is usually sterile and there may be few cells apart from red blood corpuscles. It is not unreasonable to believe that submucous or interstitial cystitis is an unresolved patch of a chronic cystitis with submucous infiltration by inflammatory cells. The explanation for the persistence of such a patch at the bladder vault may be found in the constant activity of the submucosa and the detrusor muscle at this most mobile part of the bladder wall. The fissuring with distension of the bladder leads to bleeding and a breaking down of attempts at repair with each act of filling and voiding of the bladder. (*See* Plate I(*g*).)

(*g*) *Pericystitis*

In all chronic vesical inflammations and irritations there is a fibrolipomatous infiltration in the prevesical and perivesical fasciae. Similarly pericystitis may accompany extravesical inflammations originating in the pelvic cellular tissue plane, or in adjacent organs. It is well seen in penetrating ulcers of the bladder when the organ has become contracted, as in tuberculous or interstitial cystitis. Pericystitis may become fulminant as a result of a virulent infection or ill-advised treatment by over-distension, by the use of too concentrated a chemical agent for lavage, or by careless intravesical instrumentation. A fatal

Extravasation and pelvic cellulitis

extravasation and pelvic cellulitis will occur unless immediate operative treatment is undertaken by suprapubic cystostomy and free drainage of the prevesical space anteriorly, and the pelvic cellular tissues through the perineum.

(3) Specific infections

(*a*) *Tuberculosis*

Bladder lesions secondary

In this disease the lesions in the bladder are secondary to those in the kidney or the genital tract. Tubercles appear in the bladder as a result of a secondary invasion of that organ. Just over 50 per cent of cases of genital tuberculosis in the male are associated with tuberculosis of the kidney and bladder. The

acid urines respectively. Neither is amenable to the sulphonamide drugs or penicillin. In such cases of chronic infection vesical lavage may be curative. The tidal method offers many advantages because of the constancy with which the therapeutic agent is kept in contact with the vesical mucosa. The author has found tidal lavage with 1:1,000 proflavine most helpful in cases of proteus infection, particularly in the neurogenic bladder. When there is phosphatic incrustation Suby's Solution G (1942) with the formula: Citric Acid (monohydrate) 32·25 grammes, Magnesium Oxide (anhydrous) 3·8 grammes, Sodium Carbonate 4·4 grammes, distilled water 1,000 cubic centimetres, brings dramatic relief. Solution G may be employed as a phosphatic solvent for considerable periods using the Wells tidal irrigator (*see* Fig. 35). Ionizable iodine and free urea (U.F.I.) in saturated solution yields satisfactory results in pyocyaneus infections, when it is instilled into the bladder at regular intervals and the urine is rendered alkaline (Wakeley and Blum, 1945).

Value of tidal lavage

Solution G as a phosphatic solvent

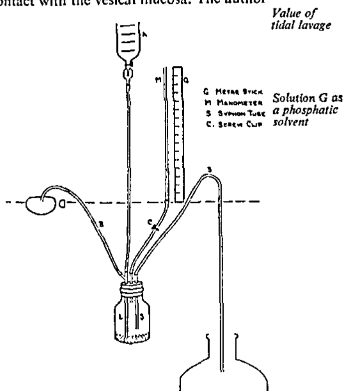


Fig. 35.—Wells Tidal Irrigator and Cystometer.

Theory and object: To connect the bladder through a closed series of tubes to irrigation apparatus, affording automatic filling and emptying (Munro, 1936).

Summary of apparatus

(1) A. A container supplying antiseptic fluid through drip.
(2) B. Connexion to bladder via catheter, either urethral or suprapubic, thence to bottle.
(3) S. Connexion to syphon, which can be placed at selected level above bladder.
(4) M. Connexion to open tube, which measures pressure (manometer) and allows air to enter circuit intermittently to break syphon.
(5) Tube from bladder (L) is longer than tube from syphon (S), and is permanently sealed beneath level of fluid in bottle. Bottle should be small to avoid slow periodicity.

Interstitial cystitis or Hunner's ulcer has been treated by overdistension of the bladder under anaesthesia, protein-shock therapy, and endoscopic fulguration of the ulcers. Of these, fulguration under anaesthesia followed by silver nitrate instillations to the bladder seems to offer the most satisfactory results. Presacral neurectomy has been found to give temporary relief (Learmonth, 1931b). Recently antero-lateral cordotomy has been used with some success (Nesbit, 1947). The multiplicity of the forms of treatment advocated and employed in this distressing condition is an indication of the rather unsatisfactory nature of any of them (Cristol, Greene and Thompson, 1944).

Fulguration in Hunner's ulcer

Tuberculosis of the bladder secondary to renal tuberculosis is the perfect

Tuberculosis

Terminal haematuria

towards the base. Haematuria is most evident towards the end of micturition; occasionally it is profuse, as in the ulcerative and incrusted forms of chronic cystitis. Urgency may be commanding, yet there is always awareness of the desire to micturate and the frequency is not to be confused with incontinence.

7. SPECIAL CONSIDERATIONS IN DIAGNOSIS

Importance of clinical methods

The history of the illness, the clinical examination and the ordinary side-room examination of the urine should provide pointers to a correct diagnosis in the majority of cases. It is of the greatest importance to consider the aetiology of a given case of cystitis, and to determine the predisposing factors. The reaction of the urine, its odour and colour, and the stained film of the centrifuged deposit, yield information of diagnostic value. The acute suprapubic pain of the distending bladder in interstitial cystitis, the relief following the act of micturition, and the absence of pus cells from the urine, form a characteristic syndrome. Conversely, an increasing frequency in a young adult, with pyuria and no organisms, are observations typical of tuberculosis. An alkaline urine, intermittent attacks of haematuria, and the occasional passage of phosphatic debris with mucus, are commonly found in incrusted cystitis.

Simple urine analysis

The combination of a clinical history, clinical examination, laboratory investigation of the urine, and radiographic studies to exclude stone, are essential preliminaries to instrumental examination by cystoscopy. Thus the changes seen in the bladder mucosa may be immediately correlated with the knowledge already gained. Cystoscopy should be regarded as the confirmatory special examination and not the preliminary to any. In the acute phases of cystitis with systemic upset, and a tender and friable bladder mucosa, instrumental examination is harmful and should be postponed until the symptoms have subsided. Then cystoscopy is carried out with a view to excluding any underlying condition, such as diverticulum, calculus or neoplasm, which may have predisposed to vesical infection and would lead to a recurrence.

Data necessary prior to cystoscopy

Instrumentation avoided in acute phase

8. TREATMENT

The immediate treatment of the symptoms of cystitis is of secondary importance to the recognition of the underlying cause and its elimination wherever possible. The general principles of rest, a bland diet and abundant diuresis still hold. The bacteriological examination of the urine is of greater importance than ever, owing to the facilities offered by the bacteriologist for the assay of the sensitivity of any strain of organism to drugs of the sulphonamide group, or to penicillin. By and large a varying degree of sensitivity to the sulphonamide drugs will be found in organisms in the *B. coli* group, and most of the pyogenic cocci are penicillin sensitive. *B. coli* flourish in an acid urine and the sulphonamide group are most efficacious in an alkaline medium in which precipitation is less likely to occur (Ainsworth-Davis, 1945). Citrate of potash with belladonna remains the standard urinary sedative, in combination with a sulphonamide drug in *B. coli* infections; whereas a urinary acidifier, such as ammonium benzoate or ammonium chloride, is prescribed with penicillin in those cases in which pyogenic cocci are found in an alkaline urine (Cruikshank, 1945). *B. proteus* and *B. pyocyaneus* occur in alkaline and

Importance of accurate bacteriological studies

Reaction of urine with sulphonamides

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[Reference to other titles are given under Bladder—*Infections* in the Index Volume. The subject of Cystitis is also dealt with under the heading of Bladder Diseases in the *British Encyclopaedia of Medical Practice* (1936), Vol. 2, p. 374.]

example of the necessity for treatment of the primary condition as an essential preliminary to therapy directed towards the bladder. Urinary tuberculosis, however, may be accompanied by extra-urogenital lesions which may offer a contra-indication to surgical intervention. Similarly, genital lesions in urogenital tuberculosis present factors which may delay extirpation of the kidney or the epididymis on account of sinus formation and secondary infection. It is a safe rule to review the patient as a whole and observe the effects of rest in bed under a sanatorium regimen. If it is considered that the primary lesion is limited to one kidney, and no active extra-urogenital lesions are demonstrable, nephrectomy may be undertaken with confidence. The treatment of genital tuberculosis is, generally speaking, conservative. Abscess formation in the epididymis and the threat of sinus formation may warrant epididymectomy in selected cases. With the primary focus in the urogenital system eradicated, the tuberculous bladder may be expected to respond to sanatorium treatment alone within six months or a year in over 60 per cent of cases. It is not advisable to attempt to hasten the resolution of the vesical lesions by local treatment, and the conservative measures of the sanatorium regimen are preferable to instillations of carbolic acid lotion or other antiseptics to the bladder.

Sinus formation and secondary infection

Nephrectomy the treatment of choice

Post-operative sanatorium treatment essential

9. PROGNOSIS

Vesical infections are readily amenable to treatment when a satisfactory cause for their origin can be ascertained and eliminated. Thus, in the female, infections and displacements in the genital tract can usually be recognized and treated and recurrence of vesical infection prevented. In the male, obstructive factors in the urethra or the bladder neck are the common causes of urinary infection, and must be dealt with. A normal metabolism, an acid urine, free urinary drainage aided by chemotherapy and the application to clinical use of new combinations of antibiotics, e.g. streptomycin, should render the prognosis in vesical infections uniformly good (Helmholz, 1945).

In this respect it should be noted that streptomycin is more effective in an alkaline medium, and that the initial dosage of streptomycin should be high, otherwise susceptible organisms become resistant to the antibiotic substance (Knop, 1946). Streptomycin has proved a useful bactericidal agent in the urinary tract infections of the paraplegic. Again the tendency to resistance of the organisms to the antibiotic agent has been noted, and a high initial dosage would appear to be essential (Petroff and Lucas, 1946).

Streptomycin may prove a useful adjuvant to surgery in the treatment of urogenital tuberculosis (Cook, Greene and Hinshaw, 1946).

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(1) Rupture of the bladder

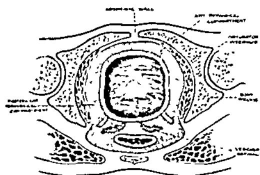


Fig. 36.—Transverse section through the pelvis to show relations of the bladder.

Direct violence

Intraperitoneal rupture most commonly results from a blow or a kick on the lower abdomen when the bladder is distended; a sudden rise in intravesical pressure precedes rupture. It is not uncommon in intoxicated persons when the abdominal muscles may be off their guard at the time of the blow. Extraperitoneal rupture frequently complicates a fracture of the pelvis. The bladder is usually torn as a result of the displacement of the fragments of bone. A distended bladder may be ruptured as a result of muscular violence, for example, the lifting of heavy weights, and straining under an anaesthetic. The bladder may be ruptured when over-distended with fluid during cystoscopy. The bladder wall may be accidentally penetrated by a lithotrite or by a per-urethral prostatic resectoscope.

Fractured pelvis

Muscular violence

Over-distension with fluid

Spontaneous rupture

Rupture may occur spontaneously or following minor injury in cases in which the bladder wall itself is the seat of disease, for example, severe cystitis, tuberculosis or carcinoma; spontaneous rupture occurs occasionally in patients with a thin-walled chronically over-distended bladder resulting from urethral obstruction; it occasionally complicates tabes dorsalis. It has occurred in the process of manual expression of urine for retention due to spinal cord injury.

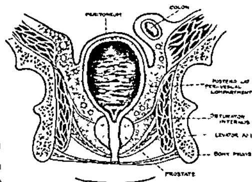


Fig. 37.—Coronal section through the pelvis to show relations of the bladder.

(2) Penetrating wounds of the bladder

War injuries

Penetrating wounds occur most commonly in war injuries from bullets or fragments of bomb or shrapnel. Stab wounds from bayonet or knife injuries occur occasionally. The base of the bladder has been penetrated during attempts to procure abortion.

Abortion

Injury during operations

The bladder may be injured during operations for femoral or even direct inguinal hernia, in operations upon the uterus or the rectum, or during laparotomy.

3. SURGICAL ANATOMY

(1) Anterior relations of the bladder

The distended bladder

As the bladder distends it becomes partly an abdominal organ, and its upper part is then protected anteriorly only by the muscles of the abdominal wall

BLADDER INJURIES

By L. N. PYRAH, Ch.M., F.R.C.S.
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Consulting Surgeon, St. James's Hospital, Leeds

1. DEFINITION

55.] Injuries to the bladder include ruptures and penetrating wounds. Ruptures occur usually as a result of trauma, but occasionally they occur spontaneously in a diseased or obstructed bladder.

2. AETIOLOGY

Age, sex Bladder injuries are most common in males between the ages of twenty and forty though no age is excluded. War injuries and accidents during games account for the high incidence in this age-group.

(2) Penetrating wounds

Route of the missile · *Fracture of pelvis* · *The bladder wound* · *Associated injuries*

A stab wound of the suprapubic region or of the perineum may penetrate the bladder. The majority of penetrating wounds of the bladder caused by bullets or metal fragments are associated with wounds of the buttock (75 per cent in Fullerton's series). More rarely the wound of entry is in the groin, the sacral region, the iliac fossa, the loin and the perineum. The external wound is often small but it communicates with the bladder cavity by a long, and often tortuous track along which urine may escape to the exterior. The pelvic bones may be splintered and fragments of bone may enter the bladder cavity. The wound in the bladder varies in size from a puncture or small tear to a large wound destroying an extensive part of the bladder wall. There may be a second wound of exit. The wound may be intraperitoneal, when the small intestine or colon are commonly injured, resulting in faecal fistula or peritonitis; or it may be extraperitoneal, when the rectum is often torn. The missile frequently lodges in the pelvis and may come to rest within the bladder cavity. The other changes follow closely those described for ruptured bladder.

5. CLINICAL PICTURE

(1) Intraperitoneal rupture

Onset · *Clinical cou* · *Physical sig*

Following a blow on the abdominal wall the patient experiences a sensation of something having given way in the abdomen, and this is followed by lower central abdominal pain. Shock may be well marked or completely absent. There is great desire to pass urine with inability to do so; alternatively, a few drops of blood-stained urine are passed. Usually the symptoms and signs of peritonitis appear early but may be delayed for several hours. Some cases show no signs of peritonitis even after three days, and in a few cases, for example those with spinal injury, death occurs from toxaemia without signs of peritonitis. In the absence of severe shock, the abdomen is rigid and tender on palpation and after several hours it becomes distended. Dullness on percussion in the region of the bladder is absent. On rectal examination the pouch of Douglas is distended.

(2) Extraperitoneal rupture

Clinical course · *Physical sig* · *Infective changes*

Shock is usually marked especially in cases with an associated fracture of the pelvis. The patient experiences severe lower abdominal pain which may radiate to the back, thighs, perineum and penis. There is an urgent desire to micturate with inability to do so, except in the case of small ruptures, when a little blood-stained urine may be passed. On examination there is localized rigidity and tenderness in the suprapubic region. As the extravasation of urine increases a palpable induration is found in the deeper layers of the lower abdominal wall. On rectal examination there may be a boggy swelling caused by extravasation of blood and urine between the base of the bladder and the rectum. If the patient is not operated upon, the signs gradually change to those of a pelvic and retroperitoneal cellulitis accompanied by profound toxaemia. Localized tenderness, and later, collections of pus or even fistulae, may appear in the buttock, in the upper and inner parts of the thigh and in the scrotum.

and not by bone; it is thus more liable than is the empty bladder to injury by blows or by penetrating missiles.

(2) The perivesical space

Compartments The perivesical space between the bladder wall and the pelvic fascia is conveniently divided into an anterior compartment, the space of Retzius, and two postero-lateral compartments, all of which intercommunicate freely. The extent and disposition of the perivesical space determine the direction taken by the extravasated urine in extraperitoneal rupture. The perivesical space is traversed by the superior and middle vesical arteries and by numerous veins, some of which may be torn in bladder injuries, resulting in the formation of an extensive haematoma.

4. MORBID ANATOMY

(1) Rupture of the bladder

Partial rupture Partial rupture occasionally follows a blow on the abdomen or the penetration of the missile close to the bladder wall.

Complete rupture In complete rupture, which is most common, urine escapes from the bladder and infection usually follows. With a large rent, the bladder empties rapidly and remains in a state of contraction. With a small rupture, some urine may remain in the bladder, being slowly expelled through the rent.

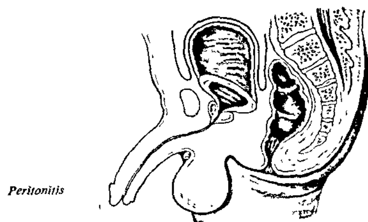


FIG. 38.—Sagittal section of the pelvis to show liability to rupture of a distended bladder as a result of a blow in the antero-posterior direction. The figure shows the bladder before and after distension (after Sandrey).

(a) Intraperitoneal rupture

Peritonitis This is usually either a vertical or a transverse tear on the dome or the posterior surface of the bladder. Blood-stained urine escapes into the peritoneal cavity. Peritonitis develops after a varying period, which is usually very short.

(b) Extraperitoneal rupture

The tear is found on the anterior or lateral wall of the bladder, or low down on the posterior wall or base. Rarely, a tear which is mainly extraperitoneal also communicates with the peritoneal cavity. Blood-stained urine distends the anterior or postero-lateral perivesical compartments and passes into the retroperitoneal tissues; the triangular ligament prevents its downward spread. As might be expected with an acid fluid a spreading pelvic cellulitis

Pelvic cellulitis develops. In late cases collections of pus may form near the bladder and infected urine may track outside the pelvis, through the sciatic foramen into the buttock, through the obturator foramen into the upper and inner part of the thigh, or along the spermatic cord into the scrotum. Pus and urine may

Late sequelae eventually be discharged through a fistula on the surface of the body. Later, thrombophlebitis, embolism and septicaemia may occur.

small or because it is temporarily plugged by a retained missile or a piece of bone, urinary extravasation occurs so slowly as to make recognition of the true state of affairs difficult and even to cause the surgeon to reject a diagnosis of bladder injury. In such cases some of the aids to diagnosis described below may be found useful. *Doubtful cases*

(1) Catheterization

If injury to the bladder is suspected, a catheter is passed. The withdrawal of a small quantity of blood-stained urine supports the diagnosis of rupture. Occasionally, the catheter may enter the peritoneal cavity through a rupture and urine may escape.

(2) Radiography

A skiagram of the pelvis will reveal fractures and retained missiles. The diagnosis of ruptured bladder has been made by an excretory skiagram. Cystography, after filling the bladder with an opaque medium, has been successfully employed but is not recommended owing to the likelihood of further extravasation. Injection of air into the bladder has been used in order to demonstrate a subphrenic air-bubble on the skiagram and also to obliterate liver dullness on percussion. This procedure is not recommended owing to the risk of shock and air embolism.

(3) Examination of escaping fluid

Fluid escaping from a penetrating wound may be proved to be urine by chemical examination; blue discoloration of the fluid after intramuscular injection of indigo-carmine is also confirmatory.

(4) Cystoscopy

Cystoscopy is not indicated in the majority of cases since the bladder cannot be distended. In some cases cystoscopy has revealed small wounds plugged by foreign bodies, bullets or fragments of shell.

(5) Injection of a measured amount of fluid

A measured amount of sterile saline has been injected into the bladder *per urethram* in order to see if a smaller quantity can be recovered. Such a procedure, which carries with it the possibility of spreading infection, can rarely be justified.

7. DIFFERENTIAL DIAGNOSIS

(1) Abdominal injury with retention of urine

In some cases of abdominal injury, and of fractured pelvis, retention of urine occurs without any injury to the bladder. Percussion of the distended bladder may be unreliable owing to the presence of extravasated blood in the suprapubic region. In such cases clear urine is withdrawn on passing a catheter.

(2) Ruptured urethra

The injury is usually a fall astride a blunt object, or a kick or blow in the perineum. There is a swelling in the perineum or bruising in front of the anus and blood at the external meatus. In complete rupture there is retention of urine. A catheter cannot be passed into the bladder along the urethra except in incomplete rupture.

(3) Penetrating wounds

Associated injuries

In war wounds involving the bladder the clinical picture is often complicated by injuries to the intestine, rectum, prostate, urethra, pelvic bones and great vessels and nerves. The clear-cut distinction between the intraperitoneal and extraperitoneal ruptures of the bladder of civil injuries is often lost. It is usually possible to reconstruct the track of the missile and this will assist in the diagnosis of possible visceral injuries.

Haemorrhage

Shock may be absent when the bladder alone is wounded, but with extensive damage to the pelvic bones or the intestine, shock is usually profound. Pain is usually experienced at the time of infliction of the wound but later may not be severe. Blood or urine may escape early from the wound, and secondary haemorrhage may take place after some days. Damaged tissue, blood clot or prolapsed intestine may prevent the escape of urine from the wound for several days. When the rectum is wounded, urine may escape from the rectum by a recto-vesical fistula, or faeces and urine together may be discharged from the parietal wound. Rectal examination may reveal the position and the extent of the wound in the rectum. Apart from the special features just described, the symptoms, signs and subsequent course are those of intraperitoneal or extraperitoneal rupture of the bladder.

Associated injury of rectum

(4) Wounds occurring during operation

Wounds from over-distension

In wounds of the bladder resulting from over-distension with fluid or from instrumental injury during intravesical procedures, the rupture may be either intraperitoneal or extraperitoneal. If the operation is being done under local or low-spinal anaesthesia sudden pain is complained of. It is usually impossible to recover through the cystoscope all the fluid which was passed into the bladder to distend it; in addition there may be unexpected haemorrhage.

Wounds during operation for hernia

Wounds of the bladder occurring during open operations are usually recognized at the time, since urine escapes into the wound. If the bladder is included in a ligature when transfixing and tying a femoral hernial sac, the first symptom may be haematuria and this may lead the surgeon to reopen the wound. In other cases, wound infection and ultimately urinary fistula may occur.

(5) *Spontaneous rupture*

Symptoms

Spontaneous rupture of a diseased or obstructed bladder may be intraperitoneal or extraperitoneal. A usual history is that the patient has developed acute retention of urine, and is in considerable discomfort, when he experiences a sensation of something having given way in the abdomen. He then develops the characteristic symptoms and signs of rupture of the bladder.

6. SPECIAL AIDS TO DIAGNOSIS

Catheterization

A bladder injury is a surgical emergency demanding immediate operation. The diagnosis, therefore, should usually be made after careful clinical examination, using only the simplest aids to diagnosis, such as the passing of a catheter. In cases of doubt the surgeon should err in favour of exploratory operation rather than invite disaster by delay. There is, however, a small proportion of cases of bladder injury in which, either because the wound is

peritoneum and the perivesical fat, and since it will have contracted down into the pelvis and be obscured by sodden and bruised tissue planes, the dissection is not easy. The rupture is sought first on the anterior, then on the lateral surfaces. The general principles described above are then applied. It may be impossible to excise wounds low down on the lateral surface. When no tear is found on the anterior and lateral walls the bladder is opened by a vertical suprapubic incision, after introducing stay-sutures through the bladder wall, in order to search for a rupture of the base of the bladder. An illuminated retractor is introduced into the bladder cavity to demonstrate the tear. Excision of the bladder wound is not practicable. If the wound can be sutured without undue tension, this should be done; but owing to the immobility of the base of the bladder consequent upon its deep relationships, suturing is frequently unsatisfactory and the wound should often be left unsutured. Free suprapubic drainage should be provided. Many such cases recover.

Rupture of anterior and lateral walls

Rupture of base of bladder

(c) *Penetrating wounds*

In cases of an intraperitoneal wound a free abdominal incision should be made and any associated injury of the small intestine or colon should be dealt with. The wound in the bladder is located and the bladder cavity explored digitally for retained missiles and pieces of bone. Search should be made for a possible wound of exit, bearing in mind that this may be extraperitoneal. The principles of treatment are then applied. In cases in which there appears to be only an extraperitoneal wound, the surgeon should satisfy himself that there is no intraperitoneal damage, and this may entail opening the peritoneal cavity through a separate incision. In some cases of wounds of the anterior wall of the bladder there may be much destruction of the bladder wall itself, and the pubic bone may be badly splintered. In order to prevent sequestrum formation and persistent cystitis in such cases, the bladder should be allowed to drop back into the pelvis after repair, and if possible fat should be interposed between the sutured bladder and the os pubis. The suprapubic drain should leave the bladder as far from the os pubis as possible (Macalpine, 1944). In wounds of the base of the bladder in which the rectum has also been injured, the resulting fistula often closes spontaneously after a time; no attempt, therefore, should be made to repair the fistulous opening but a colostomy should be made through a separate incision.

Intraperitoneal wounds

Foreign bodies

Extraperitoneal wounds

Associated bone injury

Vesico-rectal fistula

10. POST-OPERATIVE CARE

When possible, the bladder should be kept dry by suction-drainage using a Stedman's tube and pump. This method, in addition to being comfortable for the patient, largely prevents the leakage of urine into the perivesical tissues. The drain in the perivesical space or peritoneal cavity should be gradually shortened, and removed on or about the third day. The suprapubic tube should be replaced by a rubber catheter on the sixth day, and this should be retained until the wound is healed round the catheter. During all this time the bladder is frequently irrigated through the suprapubic tube with boric lotion. When the suprapubic catheter is finally removed, a Hamilton Irving belt is applied, and a catheter is tied in the urethra until the wound is dry. The sulphonamides are used freely as urinary antiseptics.

(3) Ruptured kidney

There is a history of an injury in the loin followed by haematuria. The patient is able to pass urine unless there is clot retention which will be disclosed by catheter. Examination reveals tenderness and rigidity in the loin and sometimes a tumour resulting from extravasated blood.

8. PROGNOSIS

Associated injury to the intestine or blood-vessels always carries a grave prognosis; very few such patients survive. Early diagnosis and prompt treatment on the principles to be laid down are the indispensable factors in saving life. *Urinary sepsis* Urinary sepsis may be responsible for early fatality; later chronic cystitis, fistula and calculus formation may lead to prolonged invalidism. In penetrating wounds, associated injury to the pelvic bones may lead to necrosis which may in turn help to perpetuate bladder infection and a fistula.

9. OPERATIVE TREATMENT

Immediate operation

The only contra-indication to immediate operation is shock, which calls for counter-measures to render the patient fit.

(1) Principles of operative treatment

The following principles are generally applicable to the treatment of bladder injuries; they cannot always be fully applied in practice on account of anatomical considerations, and modifications may then be called for.

Excision and suture of bladder wound

(a) The wound in the bladder wall should be excised and sutured with interrupted catgut stitches going down to, but not through, the mucosa, and tied without undue tension. A second row of sutures enfolds the first layer.

Drainage of bladder

(b) Free drainage of the bladder cavity should be provided by a wide-bore rubber tube introduced suprapubically. A de Pezzer catheter and an indwelling catheter are both unsuitable since blood clot may temporarily obstruct the opening, thus placing undesirable tension upon the sutures in the bladder wound. An escape of urine into the perivesical tissues may result.

Drainage of perivesical space

(c) A drainage tube is placed in the perivesical space adjacent to the bladder wound to prevent accumulations resulting from a leakage of urine.

(2) Operative technique

(a) Intraperitoneal rupture

The abdomen is opened by a midline incision below the umbilicus, and *Technique* urine, blood clot and pus are removed by suction. The patient is placed in slight Trendelenburg position and the intestines are packed upwards with large, hot, moist swabs. The wound in the bladder is excised and sutured. The surgeon should satisfy himself that the other abdominal viscera are *Drainage* uninjured. The peritoneal cavity is closed with a rubber drain to the pelvis. The bladder is drained suprapubically and the abdominal incision is closed.

(b) Extraperitoneal rupture

Exposure of bladder

A suprapubic midline incision is made to expose the bladder. Urine and blood are removed by suction. The bladder is exposed by stripping back the

BLADDER—NEUROGENIC DISTURBANCES

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1. ANATOMY AND PHYSIOLOGY

56.] The following account is based upon an investigation of normal and abnormal function made by Denny-Brown and Robertson (1933 a and b). The writers considered that sensory terminals in the vesical wall are stimulated by stretch, and that contraction of the vesical musculature occurs as a reflexly

11. RESULTS OF SURGICAL TREATMENT

Ruptured bladder

Gunshot wounds

Bacon (1943) recorded 147 cases of ruptured bladder with a mortality of 44 per cent. Fullerton (1918) recorded a series of 53 cases of gunshot wound of the bladder in the 1914–18 war with a mortality of 30 per cent. Only 4 patients returned to duty. A short series of cases recorded during the recent war gives hope of improved results with the assistance of modern advances in treatment.

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[References to other titles are given under Bladder Injuries in the Index Volume. The subject of Bladder Injuries is also dealt with under the heading of Bladder Diseases in the *British Encyclopaedia of Medical Practice* (1936), Vol. 2, p. 374.]

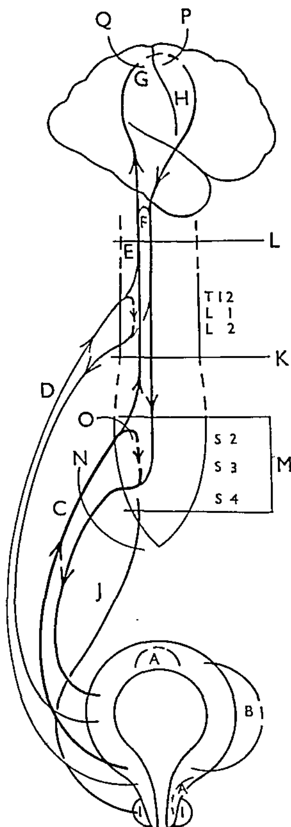


PLATE II.—Diagram of nerve supply of the bladder. The bilateral symmetry of the supply, the nerve cells and the sympathetic ganglia are not represented.

A = neurones in the vesical wall
B = reflex arcs through the pelvic plexuses
C = sacral reflex arcs—including afferent and efferent axons (pelvic nerves)
D = lumbar reflex arcs—including afferent and efferent axons (hypogastric nerves)
E = sensory axons ascending in the spinal cord
F = reflex arcs through brain stem
G = axons terminating in the parietal lobe
H = efferent axons originating in the frontal lobe
I = external vesical sphincter
J = pudendal nerve
K = transverse lesion of cord between lumbar and sacral outflows
L = transverse lesion above lumbar outflow
M = lesion of sacral segments of cord
N = lesion of pelvic and pudendal nerves (cauda *equina*)
O = lesion in root entry zone
P = lesion in frontal lobe
Q = lesion in parietal lobe
T12 = twelfth thoracic segment of the spinal cord
L1 = first lumbar segment
L2 = second lumbar segment
S2 = second sacral segment
S3 = third sacral segment
S4 = fourth sacral segment

PLATE II

induced response. The reflex arcs concerned are, however, subject to restraint from higher levels of the nervous system. Thus the bladder is thought to be influenced by activating and controlling reflex arcs.

(1) Activating reflex arcs

These may be divided into two groups:

(*a*) *Peripheral reflex arcs*

Tonic and phasic vesical contractions

The neurones are situated in the vesical wall and neighbouring pelvic plexuses (Plate II A and B). Denny-Brown and Robertson believed that these cause sustained (tonic) and intermittent (phasic) contraction in response to distension. In order to act as a distendable reservoir the bladder wall must be capable of covering a larger area, that is to say, a process of adaptation to enclosed volume must be possible. When the bladder is isolated from the central nervous system adaptation is poor, apparently because inhibitory restraint is absent. The capacity of the bladder is small, and the intravesical pressure rises rapidly during distension. As filling proceeds, small phasic contractions of brief duration are superimposed upon the background of tonic contraction. The phasic waves are poorly co-ordinated and do not summate into large contractions. Brief pressure applied passively through the abdominal wall may be used to sample the "stretch response", and, in this instance, produces a small contraction of brief duration.

Stretch response

The peripheral reflex arcs correlate the vesical musculature with the relaxation of the urethral orifice. When the vesical wall is relaxed the latter is tightly contracted. As the bladder contracts the sphincter becomes more and more relaxed. There is no doubt of the existence of a sphincteric effect which is not directly under voluntary control, whether it is due to a circular band of smooth muscle, or to fibres so arranged that contraction causes opening of the orifice by funnelling of the proximal urethra.

(*b*) *Spinal reflex arcs*

Parasympathetic and sympathetic outflows

Afferent fibres pass to the second, third and fourth sacral segments, whence efferent parasympathetic fibres pass to the bladder via the pelvic nerves (Plate II C). Reflex arcs also pass through the eleventh and twelfth thoracic and first lumbar segments. The efferent fibres, passing via the hypogastric plexuses and nerves, constitute the sympathetic outflow (Plate II D).

The doctrine that the two outflows are mutually antagonistic is probably incorrect. It seems that both outflows produce the same effect, although the sacral outflow is far more important than the lumbar.

Observations made upon patients with destruction of the spinal cord above the sacral segments (Plate II K and L), suggest that these spinal reflex arcs cause integration of the vesical contraction. The bladder adapts itself to a small volume only, and then contracts strongly and as a whole, emptying itself more completely than the isolated bladder. Vigorous phasic contraction is stimulated by light passive pressure, and may be sufficient to cause evacuation.

(2) Controlling reflex arcs

Control is a cerebral function and is probably inhibitory in character.

(*a*) *Afferent fibres*

Fibres conveying information to the brain ascend in the spinal cord, probably chiefly in the posterior columns (Plate II E). Some of the axons probably

relay in the brain-stem (Plate II F), while others reach the parietal lobe (Plate II G) and subserve consciousness of vesical distension and desire for micturition.

(*b*) *Efferent fibres*

The reflex arcs are completed by axons which probably arise in the frontal lobes, and descend in close relationship with the pyramidal tracts (Plate II H). It is believed that these connexions enable the individual to restrain micturition. In the early stages of filling, inhibition is effected unconsciously, producing adaptation to the enclosed volume. Later, as phasic contractions of greater magnitude lead to a sensation of desire for micturition, the inhibition is reinforced by conscious effort. When the individual relaxes the inhibitory control, micturition is produced by the sacral reflex arcs. *Descending fibres near pyramidal tracts*

(3) External sphincter

The external vesical sphincter (Plate II I), part of the pelvic diaphragm of voluntary muscle, is innervated by the pudendal nerves (Plate II J) from the second, third and fourth sacral segments. Sensations from the urethra and pelvic diaphragm are conveyed in the pudendal nerves. Relaxation of the sphincter precedes micturition. Willed effort produces abrupt contraction of the sphincter. If micturition is in progress the latter causes abrupt interruption of the stream, and a slow subsidence of vesical contraction follows. *External sphincter under voluntary control*

2. CLINICAL PICTURE

The effect of nervous lesions upon the bladder depends upon the situation of the lesion.

(1) Lesions of the conus medullaris and cauda equina

(*a*) *Commoner causes*

Trauma, neoplasm, myelitis, developmental defect (spina bifida).

(*b*) *Micturition*

After destruction of the sacral segments (Plate II M) or nerve roots (Plate II N) the bladder appears to function under the influence of the peripheral reflex arcs. Following an abrupt lesion, the vesical musculature becomes toneless, while the urethral orifice is closed. Eventually the peripheral reflex arcs recover sufficiently to cause extrusion of urine. The final state is similar to that produced by a slowly progressive lesion. Small volumes of urine are passed frequently due to small irregular contractions, which never coalesce into high-pressure responses. Hence the bladder does not empty. The patient is conscious of sensations from the bladder (apparently travelling via the hypogastric nerves), but does not feel the passage of urine because the pudendal nerves are interrupted. Voluntary control is greatly diminished, although the patient can influence evacuation by straining. Having experienced a sensation produced by vesical contraction, he increases the intra-vesical pressure (at a time when further phasic contractions are likely to occur). Thus he is able to cause a more forceful evacuation through the sphincter which has relaxed in proportion to the contraction of the vesical wall. He may forestall the incontinence which would result if he delayed and, in addition, the frequency of micturition is lessened, for larger volumes are passed. *Type of micturition* *Effect of straining*

Impairment of the hypogastric pathways (Plate II D) does not appear to

its tone is modified by reflexes passing through the sacral segments. The sphincter relaxes when urine passes, and stimulation of the sole of the foot may cause it to contract, thus interrupting the stream of urine (a further criticism of the theory of a "mass reflex").

(3) Diseases of the spinal cord

Analysis of causes of vesical involvement

Diseases of the spinal cord derange vesical function by involving three groups of axons; first, sensory axons as they enter the cord, secondly, ascending axons and, thirdly, descending axons. The clinical picture depends upon the fibres affected.

(*a*) *Lesions of the entering sensory axons*

Lesions in the root entry zone (Plate II O), or of the dorsal roots, involve fibres destined both for the cortex and local reflex arcs.

(i) *Impairment of cerebral afferents* (Plate II E).—The appreciation of vesical distension is reduced. In advanced lesions the desire for micturition is abolished, and the patient does not attempt to micturate (that is, to release inhibitory control) until the passage of time or a sense of abdominal fullness prompts him to do so. Impairment of the afferents may cause difficulty in releasing inhibition. Hence the bladder tends to become over-distended, and the stretching impairs the efficiency of contraction.

(ii) *Impairment of sacral reflex arcs.*—The integration effected by the sacral segments is impaired, and in advanced lesions micturition is due to peripheral neurones (Plate II A).

(*b*) *Lesions of the ascending axons* (Plate II E)

As described above, this leads to undue persistence of cerebral inhibitory dominance.

(*c*) *Lesions of the descending axons* (Plate II H)

Frequency and precipitancy due to lesions of inhibitory fibres

The cortical inhibitory outflow is impaired, hence the sacral reflex arcs tend to assume control.

Both ascending and descending fibres (Plate II E and H) may be involved together, producing loss of the inhibitory capacity together with loss of awareness of the state of the bladder.

(4) Tabes dorsalis

The entering sensory axons (Plate II O) are involved.

Initiation of micturition

Lacking the sensation of desire for micturition, the patient micturates infrequently. The excessive distension which results causes impairment of contraction. For this reason, and probably also because of lack of afferent information, he has difficulty in initiating micturition. Eventually the flow may commence without his knowledge, probably under the influence of peripheral reflex arcs (Plate II A), the sacral reflex arcs (Plate II C) having been impaired. Hence small volumes only are extruded. The patient is able to stop the flow as soon as he is aware of it, but the flow soon recommences. Consequently in advanced stages "overflow incontinence" occurs.

"Overflow incontinence"

Clinical signs

A history of "lightning" pains, reduction of deep reflexes, hypo-algesia, defective appreciation of the posture of the joints and pupillary changes serve to establish the diagnosis. The Wassermann reaction may be negative in both blood and cerebrospinal fluid.

add any essential element to the vesical abnormality although awareness of vesical distention may be lessened.

(*c*) *External sphincter*

Flaccid paralysis of pelvic diaphragm

The pelvic diaphragm is paralysed and toneless. Therefore the patient is unable to interrupt the stream of urine.

(*d*) *Comparison between lesions of conus medullaris and cauda equina*

Lesions of the sacral segments and of the emergent roots produce the same effect upon vesical function. On clinical grounds it may be difficult to determine whether the conus or roots are damaged. Compression of the emergent roots is much less serious than destruction of the neurones of the conus (for it may be removable), hence it is important to determine the level of the lesion.

(*e*) *Neurological examination*

Incomplete examination may fail to reveal evidence of a lesion confined to the second, third and fourth sacral segments or emergent roots, although the signs are striking. The perineum and peri-anal regions are anaesthetic. The pelvic diaphragm, with its sphincters, is paralysed. The patient cannot retract the perineum, which bulges on coughing. Digital examination shows that the external anal sphincter is relaxed, and it does not contract in response to voluntary effort, to movement of the intruding finger, or to scratching of the peri-anal region. If the lesion involves higher segments, muscular weakness with diminution of reflexes and sensations are obvious in the lower limbs.

Signs of more widespread lesions

(2) Interruption of spinal cord above the sacral segments (Plate II L and K)

(*a*) *Commoner causes*

Trauma, neoplasm, vertebral disease, myelitis.

(*b*) *Micturition*

An abrupt lesion causes retention and excessive distension of the bladder. As the bladder increases in size the mechanical pressure exerted by the stretched wall may eventually force urine past the internal sphincter. Later, or perhaps even at an early stage, evacuation of small quantities is produced by the peripheral reflex arcs. Finally, the " automatic " bladder develops, as the spinal reflex arcs emerge from the depression of shock. At this stage forceful evacuation occurs at frequent intervals, although the bladder is rarely emptied. The patient has no control over vesical activity, even when the lesion is below the origin of the hypogastric nerves (Plate II K). An unusual sensation may precede evacuation, but the patient cannot feel the passage of urine. Because of the briskness of the stretch response, pressure applied through the abdominal wall, especially if repeated, may stimulate evacuation. A brisk flexion response produced by plantar stimulation may include contraction of the abdominal and perineal musculature. The vesical contraction induced may be sufficient to produce evacuation. Such an evacuation is not evidence of a "mass reflex".

Development of the "automatic" bladder

(*c*) *External sphincter*

External sphincter paralysed

The nerve supply from the sacral segments is intact, but the pyramidal fibres are interrupted. Hence the sphincter cannot be contracted voluntarily, while

(c) Cerebral degenerative lesions

Involvement of the frontal lobe (Plate II P) causes failure of inhibitory capacity and leads to precipitancy and incontinence. Deterioration of the cerebrum reduces the patient's desire to conform to ordinary standards of conduct.

(d) Neoplasms of the frontal lobes

Neoplastic involvement causes a similar type of disturbance.

(e) Neoplasms of the parietal lobes

A meningioma involving the upper parts of both parietal lobes (Plate II Q) may lead to loss of awareness of the state of the bladder, hence the effect is the same as that of lesions of ascending axons (Plate II E).

(f) Epilepsy

When the bladder is full involuntary evacuation, due to release of the sacral reflex arcs, may follow the abolition of cortical control. Rarely, evacuation occurs in a minor attack. The patient may be dimly aware that urine is passing, but is unable to prevent it. This suggests disturbance of the anatomical substratum of inhibition.

3. SPECIAL AIDS TO DIAGNOSIS

Examination of the urine is essential. Cystoscopy is valuable if an obstructive lesion is in question. Radiography of the spine may reveal evidence of vertebral disease, or bifid laminae. Various methods of cystometry, including a long glass tube connected to a reservoir and catheter, may be used to estimate distensibility, briskness of stretch response, and strength of vesical contraction. However, cystometry lacks value in differentiating neurological causes, for the inflamed or irritable bladder behaves in the same manner as the uninhibited bladder, and the stretched bladder of mechanical obstruction produces a curve similar to that of the hypotonic bladder.

4. DIFFERENTIAL DIAGNOSIS

Signs and symptoms of nervous disease are usually present when the cause is neurological. A detailed history of micturition may clarify the diagnosis, and render unnecessary mechanical methods of investigation. The patient frequently denies trouble in micturating, yet enquiry yields evidence of gross abnormality. The following points need to be determined: *Value of history*

Diurnal and nocturnal frequency
Amounts passed
Quality of sensation of desire for micturition
Mode and ease of starting; whether straining is necessary
Capacity for postponing micturition
Type of stream
Sensation accompanying flow
Ability to stop the stream.

The volume of residual urine may provide important information.

Rectal and sexual functions are frequently disordered when the nervous control of the bladder is impaired. Whatever the nervous lesion, there is usually constipation, with uncontrollable evacuation after purgation (Denny-Brown and Robertson, 1935).

(5) Subacute combined degeneration of the cord

The posterior columns are usually affected before the lateral columns, but in advanced cases all tracts may be destroyed.

In the early stages micturition may be normal. With impairment of the ascending fibres (Plate II E) micturition becomes infrequent and difficult to initiate. The sacral reflex arcs are intact, hence emptying is efficient until the musculature is impaired by excessive distension. When the descending fibres (Plate II H) are involved precipitancy develops, and when the tracts are completely destroyed, evacuation is forceful and uncontrolled.

Diagnosis

The presence of some of the following assist in diagnosis—peripheral dysaesthesiae, impairment of appreciation of posture of joints, loss or increase of deep reflexes, extensor plantar responses, hypochlorhydria, superficial glossitis and pernicious anaemia.

(6) Disseminated sclerosis

The descending fibres in the spinal cord are usually predominantly affected. The patient is aware of vesical sensations, but cannot inhibit the powerful contractions which occur in response to small degrees of stretch.

Frequency and precipitancy of micturition

Evacuation occurs sometimes with hesitancy and sometimes with undue frequency and little warning. Intense effort, combined with contraction of the external sphincter, may temporarily subjugate the vesical contraction. In advanced cases incontinence occurs. The patient may restrain the outflow when he stands, but movement places the pelvic diaphragm at a disadvantage and urine dribbles away.

Diagnosis

Increased deep reflexes and extensor plantar responses indicate the presence of a lesion of the upper motor neurones, which usually exists when the descending vesical fibres are involved.

(7) Syringomyelia

Precipitant micturition, with difficulty in controlling evacuation, occurs in syringomyelia and in other conditions in which the inhibitory fibres are involved, such as myelitis and slow spinal compression. Micturition is normal in amyotrophic lateral sclerosis, the vesical fibres apparently being unaffected.

(8) Neoplasms of the brain-stem

Difficulty in passing urine may be among the initial symptoms of gliomatosis of the brain-stem.

(9) Diseases of the cerebral hemispheres

(a) *Normal range of inhibitory capacity*

The ease of controlling micturition varies greatly. Some individuals restrain micturition when large volumes are present, others find difficulty in holding much smaller volumes. At one extreme of this normal range are those whose poor capacity for inhibition results in diurnal precipitancy and nocturnal enuresis.

Nocturnal enuresis

(b) *Psychological factors*

Some individuals are unable to initiate micturition when others are present. Precipitancy may occur, particularly in women, under conditions of emotional strain, or when micturition is inconvenient.

BLADDER-POUCHES

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1. DEFINITION

57.] A bladder pouch, more generally called a vesical diverticulum, is a thin-walled cavity communicating with the bladder by a narrow orifice. It is to be distinguished from the small multiple sacculations, so commonly seen in conjunction with bladder fasciculation, resulting from urinary obstruction.

2. AETIOLOGY

This is disputed. The majority of pouches are acquired conditions and result from obstruction to the outflow of urine from the bladder. About 2 per cent appear to be of congenital origin. Diverticula have been found in the foetus. The common situation of the orifice, near the ureteric openings, where that part of bladder wall which is derived from the Wolffian ducts fuses with the upper portion derived from the cloaca, is thought to indicate that a congenital weakness in this part of the bladder wall contributes to the formation of pouches.

Transient retention in the elderly male

Occasionally retention develops abruptly in an elderly patient, and investigation reveals an atonic dilated bladder, without evidence of nervous or obstructive disease. This may be due to impairment by stretching, produced by undue postponement of micturition. The vesical muscle fails to contract and the sphincter to relax. It is possible that there is a mild or transient obstructive element, for example due to hyperaemia. Repeated catheterization or injection of peripheral parasympathetic stimulants usually restores function.

Parkinson's disease

Sometimes nervous and vesical diseases coexist. Parkinson's disease does not produce vesical disorder, yet in the male sufferer retention often develops, due to hypertrophy of the prostate gland. Each is a chronic disease, occurring at the same stage of life.

5. TREATMENT

Tidal and suprapubic drainage

The object of management in severe lesions is to ensure full evacuation and to minimize infection, contracture or excessive distension. Tidal drainage is the ideal method of attaining these desiderata, although the risk of urethritis exists. If after interruption of the spinal cord, tidal drainage is impracticable, suprapubic cystotomy and drainage is the best method of avoiding infection of the bladder.

Chemotherapy

Sulphonamides are excreted in the urine, hence relatively small doses (1 gramme three times daily) may help in preventing infection. Larger doses—with due safeguards against anuria—and penicillin, are used to combat established infections.

In post-operative retention, and when the bladder is atonic, injection of carbachol may secure evacuation. Patients with tabes or subacute combined degeneration should be instructed to pass urine five or six times during the waking hours.

Tincture of belladonna (5 to 20 minims) or ephedrine hydrochloride (½–1½ grains) taken at bedtime, with endeavours to restrain micturition for longer and longer periods during the day, and attempts to interrupt the stream during micturition, may be added to the usual methods of treating nocturnal enuresis.

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— — (1935). *Ibid.*, **58**, 256.

[References to other titles are given under Bladder—Neurogenic Disturbances in the Index Volume. The subject of Nervous Affections of the Bladder is also dealt with under the heading of Bladder Diseases in the *British Encyclopaedia of Medical Practice* (1936), Vol. 2, p. 374.]

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3. SEX AND AGE

Pouches occur most frequently in males in the fifth and sixth decades. Of 236 cases, Kretschmer recorded 7 in females.

4. SURGICAL ANATOMY

Diverticula are commonly single but sometimes two or more are present. The rest of the bladder wall may be smooth; often there are some sacculi, but it is rarely intensely fasciculated and sacculated.

Orifice The orifice is small in diameter; its length is that of the thickness of the surrounding bladder wall. It is usually situated about an inch above and external to a ureteric orifice. Sometimes it is near the middle line and just behind the interureteric bar, but occasionally much farther back. Rarely it is near the apex of the bladder. A persistent urachal cyst is sometimes found in this region.

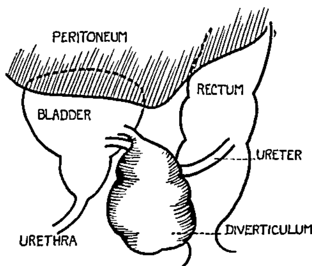


Fig. 39.—The usual relationship of the ureter to a lateral diverticulum.

Cavity The cavity is lined with smooth vesical epithelium less vascular than that of the bladder itself, unless sepsis is present when it may be replaced by granulation tissue. Its capacity may be much larger than that of the bladder.

Wall The wall is composed chiefly of fibrous tissue with a few fibres of unstriped muscle and has no contractile power.

A diverticulum, as it enlarges, descends towards the bottom of the pelvis and the main cavity comes to lie between the bladder, the rectum, the levator ani and the lateral pelvic wall; in doing so it often develops a short neck.

Neck This is closely related to the ureter over which it hangs and which it may obstruct. The most distal part of the sac is often densely adherent to

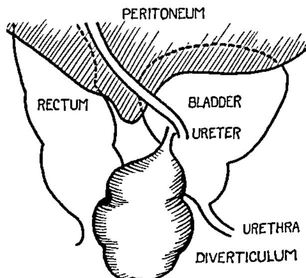


Fig. 40.—An uncommon relationship between ureter and diverticulum.

surrounding tissue. Adhesions extending towards the obturator foramen, considered to be of congenital origin, have been recognized and thought to cause traction upon this part of the bladder wall. Rarely the neck passes below the ureter. In either case the proximity of the duct is of great importance when excision of the sac is performed.

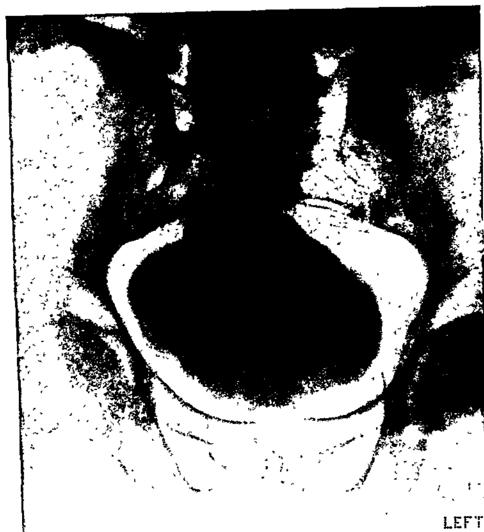


FIG. 41.—Cystogram, antero-posterior view. Bladder filled with sodium iodide solution which partly obscures the diverticulum on the right side.

5. PATHOLOGY

(1) Of the diverticulum

(*a*) *The growth of the pouch*

The urinary outflow from the bladder is impeded often by associated disease. One stimulus to the internal meatus to relax on normal micturition is a rise of intravesical pressure. When a pouch is present urine flows into it at least as easily as it can enter the urethra. One effect of this is to cause progressive increase of the sac which, having no contractile power, remains more or less

full of urine, whilst the other is, as a consequence of the resulting fall of pressure, spontaneous closure of the sphincter and hence residual urine in the bladder itself. The writer treated a patient who had no residual urine until calculi had been removed from his diverticulum which was not resected. For the remainder of his life he was catheterized once a week and had always



Fig. 42.—Cystogram, antero-posterior view. The patient has voided urine as far as he is able to do so. He is still straining in an endeavour to pass more urine; the bladder is in systole, and as a result the diverticulum is more filled than in Fig. 41.

eight ounces of residual urine, and doubtless more in the sac which was then able to accommodate urine.

(*b*) *The ureter*

The ureter may open upon the edge of the orifice; rarely it is situated inside the pouch. The neck of the sac by its relation to the ureter may cause obstruction which is sometimes sufficient to produce hydro-ureter and hydronephrosis, in which case renal infection is liable to occur.

(c) *Rupture*

This occurs rarely; it may be extraperitoneal or intraperitoneal. In either case it is serious and may cause death.

(d) *Infection*

Infection is common because of the stagnation of the urine in the sac. In 53 cases all had sepsis except 3, and in 8 it was very severe. Sepsis cannot be cured by bladder irrigations, and is not relieved but may be made worse by cystostomy.

(e) *Calculus formation*

Stagnation encourages calculus formation. In 53 patients who had vesical diverticula 2 had calculi only in the pouch, 10 had them in the pouch and also in the bladder, and in 1 the stone was in the bladder.

(f) *Neoplasm*

This may be a villous papilloma or an infiltrating carcinoma, sometimes situated at the orifice of the pouch and visible on cystoscopy, or sometimes entirely within it.

(g) *Tuberculosis and leucoplakia*

These may affect the sac.

(2) Of conditions which affect the outflow of urine from the bladder

These may take several forms and it is very important that they should be recognized since treatment is essential to ensure free micturition and to prevent recurrence. In some cases no obstructive cause can be recognized.

These conditions are placed in order according to the frequency with which they occur.

(a) *Stenosis of the bladder neck*

Stenosis interferes with the free opening of the internal urinary meatus. This condition is not easy to recognize; it may be due to hypertrophy of the internal sphincter, possibly of congenital origin, or to excess of fibrous tissue the result of local chronic inflammation or in certain instances to minimal degrees of prostatic hypertrophy. The first two forms may occur in the female and should be sought for carefully.

(b) *Benign prostatic obstruction*

The prostate may be considerably enlarged; more often, however, the enlargement is slight yet highly obstructive. There may be only hypertrophy of the middle lobe, and of a degree not easy to recognize even on cystoscopy. Occasionally carcinoma of the prostate is found.

(c) *Chronic prostatitis*

When this is the cause it is often associated with prostatic calculi

(d) *Urethral stricture*

This may affect any part of the canal.

6. CLINICAL PICTURE

Frequency of micturition

Often the sac reaches a large size without the patient being aware that there is anything the matter with him. The commonest symptom is frequency of micturition due to cystitis or prostatic changes. Pain on micturition is the next commonest; in 53 cases it was present in all but 2. Pain is also

Pain on micturition

occasionally felt in the perineum, suprapubically, or in the groin on the same side as the pouch.

Haematuria Haematuria occurs in about one-third of the number of cases, and may be due to cystitis, perhaps with calculus formation, or due to a congested prostate. A neoplasm may be the source.

Difficulty in micturition Difficulty in micturition is the most characteristic symptom; 36 of 53 patients had this, and of these, 14 had suffered from retention. The latter may be due



FIG. 43.—Cystogram showing in oblique view the bladder filled with sodium iodide solution and a diverticulum posteriorly.

to obstruction at or below the bladder neck, but the important part played by the diverticulum is mentioned above under pathology of the diverticulum.

7. DIAGNOSIS

History The history will not make this obvious. *Miction en deux temps*, a supposedly diagnostic sign, occurs also in cases of prostatic obstruction. Rarely on general

examination it may be possible to recognize two tumours rising out of the pelvis, one the bladder, the other the diverticulum.

The following investigations should be carried out. The prostate is examined per rectum and bimanually, the external urinary meatus is inspected, and the penile urethra palpated. Cystoscopy reveals the orifice of the pouch; when open this usually is smooth; when closed the mucosa is often pleated into folds radiating from it. If the urine is clean the examination usually is easy, but if it is dirty much washing out of the bladder is necessary. The use of a flushing cystoscope facilitates examination. Through it fluid can be run into the bladder during inspection, and can be continued until the suspected orifice of a pouch is caused to open; a considerable distension may be necessary. If an instrument of the McCarthy panendoscope type is available it is often possible to introduce the objective into the sac to examine the interior. The passage of a cystoscope will also bring to light a urethral stricture. The examination shows the presence of complications in the bladder, and it enables the all-important condition of the vesical neck to be determined. Some idea of the size of a pouch can be determined by noting what length of ureteric the catheter can be passed into it. *Cystoscopy*

Radiography will demonstrate calculi. A calculus seen to be in an extreme lateral position probably lies in a pouch, particularly if it retains its position after the patient has been rolled on to his opposite side and slowly allowed to return to the dorsal position. If x-rays show more stones than are counted on cystoscopy a diverticulum must be carefully sought for. Excretion urography will reveal ureteric and renal obstruction and the bladder views may show the pouch. *Radiography*

Cystography using 5 per cent sodium iodide is important. The bladder is distended with about fifteen ounces. An antero-posterior and an oblique x-ray picture are taken which will show the position and the dimensions of the pouch. The patient then micturates as completely as possible. The next x-ray picture shows the pouch still partly filled and residual urine in the bladder. A catheter is now passed and all fluid allowed to run out; the subsequent x-ray picture shows the fluid remaining in the pouch—named by Swift Joly concealed residual urine. These cystograms together with cystoscopy are also important aids in deciding upon treatment. The urine should be fully examined and the blood urea is estimated. *Cystography*

8. DIFFERENTIAL DIAGNOSIS

Accurate cystoscopy and cystography will prevent the mistake of removing an enlarged prostate and leaving a diverticulum, or removing a stone from the bladder or treating it by litholapaxy whilst another remains in a diverticulum.

9. PROGNOSIS

The pouch will gradually enlarge and infection is always likely to occur; therefore surgical treatment is indicated if conditions permit, though it may be omitted in the case of small pouches which retain little concealed residual urine and which are not infected.

10. PRE-OPERATIVE MANAGEMENT OF THE PATIENT

The less done to the bladder the better, but uraemia or gross sepsis may compel treatment by tied-in or intermittent catheterization, when bladder irrigation is essential. Cystostomy must be avoided; it does not drain the diverticulum and it makes subsequent operation more difficult, but if regarded as essential, then, in addition to draining the bladder, a second tube must be passed into the sac and stitched to its orifice, and both tubes must be irrigated frequently. Diuresis is important. Urinary antiseptics are indicated for the treatment of infection and to prevent septic complications of operation. Sulphadiazine and penicillin are of special value.

11. OPERATIVE TECHNIQUE

Measures to enlarge the orifice of the pouch are useless. Having no contractile power the pouch should be removed. Mechanical obstruction to bladder-emptying must be treated.

(*a*) *Excision of a small diverticulum*

The patient is put in a partial Trendelenburg position. The number and position of the pouches should have been carefully noted on cystoscopy for they are easily missed when the bladder has been opened. The bladder is distended with 8 ounces of lotion, the abdominal wall is entered through a 5-inch incision, the peritoneum freed upwards, a 3-inch incision is made into the bladder and the fluid evacuated with a sucker. A suitable bladder retractor is introduced, preferably one of the illuminated patterns, and the orifice and that of the ureter is identified. A small pouch is removed by cutting through the whole thickness of the bladder wall around the orifice which is picked up by long dissecting forceps. By means of a dissection with long scissors the outer surface of the sac is brought into view, and gradually it is drawn into the bladder and removed; a finger in the sac may facilitate this. The dissection is kept close to the wall of the diverticulum, and if this is done it is unlikely that the peritoneum, the ureter or the vas will be injured. When the urine is aseptic and haemorrhage is slight, the gap in the bladder wall can be entirely
Sepsis closed with sutures of No. 1 or No. 2 plain catgut. If sepsis exists a piece of corrugated rubber should be passed into the cavity from which the pouch was removed, and brought out of the abdomen beside the cystostomy tube. The bladder is always drained and the abdominal wall sutured in the usual manner.

It is dangerous to attempt to invert the pouch by seizing its wall with forceps thrust into its depths, for all sacs except the smallest are adherent to adjacent structures.

(*b*) *Excision of a large diverticulum*

A large diverticulum requires more dissection. Before opening the bladder it is widely cleared by dissection with the fingers on the side of the diverticulum, the peritoneum being pushed upwards, which brings some part of the sac into view. The bladder wall is incised near the vault and the incision is prolonged laterally down towards the orifice of the pouch. A retractor is introduced, and the exact position of the orifice is determined. It is often wise
Incision to pass a ureteric bougie for a full distance up the adjacent ureter. The incision

is now carried round and close to the opening of the sac which is thus entirely detached from the bladder. Forceps are attached to the sac and, aided by a finger inside, it is freed by means of dissection with gauze and scissors, always keeping the dissection close to the wall of the sac. There are often dense adhesions in the deepest parts. It is immaterial if the sac is accidentally opened; haemorrhage is not usually severe. The lateral incision in the bladder wall is closed with interrupted sutures of No. 2 plain catgut, care being taken not to compress the ureter. A cystotomy tube is introduced and a ½-inch drainage tube placed outside the bladder, reaching into the depth from which the pouch was removed. Calculi are removed at the same operation, also neoplasms, or the latter are destroyed by diathermy. *Cystotomy tube*

The chief danger to be avoided is injury to the ureter, an accident which may be prevented by having a bougie within it. Care must be taken to avoid compressing it by sutures when closing the lateral bladder incision. If the ureteric orifice lies within the sac the ureter must be dissected free and re-implanted. *Danger*

(c) *Treatment of bladder-neck and other obstructions*

At the operation the internal urinary meatus should always be inspected to recognize any degree of prostatic enlargement; it should also be examined by a finger tip passed into it to recognize stenosis if it is present. The treatment of these conditions is essential if a full cure is to be obtained. It is usually best to postpone this until a fortnight after diverticulectomy. Urethral stricture may also need to be dealt with.

12. POST-OPERATIVE CARE UP TO CONVALESCENCE

The bladder is irrigated twice daily for the first week, by which time the extravesical tube has been shortened gradually and removed. The cystotomy tube is retained until any treatment of the vesical neck is completed; then it is removed and a catheter tied into the urethra and kept in position until the bladder is closed, irrigation being continued twice daily. Abdominal distension may be troublesome. Diuresis must be maintained.

13. RESULTS OF TREATMENT

If a diverticulum is excised and a vesical-neck obstruction removed, the results are good. Sepsis disappears or diminishes and symptoms are relieved. In a few cases diverticulectomy cannot be undertaken because of the patient's feeble condition. It may sometimes be justifiable only to remove calculi, but in such cases sepsis is likely to persist and stones to re-form. In the case of small diverticula it may be desirable to treat only the vesical-neck obstruction by one or other form of perurethral resection.

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[References to other titles are given under Bladder Pouches in the Index Volume. The subject of Diverticulum is also dealt with under the heading of Bladder Diseases in the *British Encyclopaedia of Medical Practice* (1936), Vol. 2, p. 374.]

BLADDER—TUMOURS

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1. DEFINITION

58.] Tumour implies a neoplasm arising in the bladder itself (primary) or invading it from without (secondary).

2. AETIOLOGY

The cause is unknown. Infection plays little part, the commonest tumour, the papilloma, appearing first in an uninfected bladder. Leucoplakia, associated with chronic infection, tends, however, to become epitheliomatous. Bilharzial cystitis is frequently the precursor of new growth. Irritation may produce the papillomata observed in aniline dye workers. Apical tumours may arise in persistent remnants of the urachus.

Papilloma occurs commonly from 20 to 50 years of age, carcinoma after 40. The average age in 100 cases was 61·5 years. Sarcoma attacks infants. *Age*

Men are affected 4 times more often than women. *Sex*

3. SURGICAL ANATOMY

The fundus, covered by peritoneum, is mobile, and a growth here is accessible for excision, but prone to give peritoneal secondaries.

The arterial supply comes from the superior and inferior vesical branches of the internal iliac artery.

The lymphatic drainage is into the iliac glands.

The ureters open into the angles of the trigone at the base. A tumour at a ureteric orifice may obstruct it, and will demand re-implantation of the ureter if excised.

The base is fixed; in the male the prostate surrounds the internal meatus, and infiltrating growth here can be adequately removed only by total cystectomy and prostatectomy. Behind the base are the seminal vesicles which separate it from the rectum.

In the female the base is close to the anterior vaginal wall and cervical part of the uterus; carcinoma of the cervix may spread into the bladder.

4. PATHOLOGY

Tumours of the bladder arise in connective or epithelial tissue, and may be benign or malignant; the distinction between innocency and malignancy is less clear than in other parts of the body.

(1) Connective tissue tumours

These are rare; all types occur, but of the benign tumours angioma, either capillary or cavernous, is the commonest. Spindle-cell sarcoma of infants is of rapid growth, sometimes projecting from the female urethra. It usually produces death from urinary obstruction and infection before blood-borne metastases are evident. *Angioma and sarcoma*

Osteogenic sarcoma has also been recorded.

(2) Epithelial tumours

There is a marked tendency for all bladder tumours to become malignant.

(*a*) *Primary* *Classification*

- (i) *Papillary*
- (ii) *Nodular*
- (iii) *Ulcerating*
- (iv) *Adenocarcinoma*
- (v) *Endometrioma*

(*b*) *Secondary*

- (i) *Spread from other parts of the urinary tract*
- (ii) *Extensions from extra-urinary sources*

(i) *Papillary tumours.*—Villous papilloma in its early stages is a benign tumour, but is potentially malignant, and not only grows in size but may change into a papillary carcinoma. *Villous papilloma*

In its earliest stage a papilloma consists of a small red elevation on the

bladder mucosa. Soon villi can be detected, long branching finger-like processes springing from a relatively narrow pedicle. Each process contains central blood-vessels in a minimum of stroma covered by transitional epithelium. Its vascularity gives it a bright cherry-red colour which contrasts with the yellowish-pink of the bladder mucosa.



FIG. 44.—Diffuse papillary carcinoma infiltrating the bladder wall. Total cystectomy specimen.

Features of malignancy

In course of time the papilloma becomes larger, the main increase affecting the periphery so that the pedicle remains relatively short. The villi then tend to shrink and become stunted, stubby and closely packed, the surface of the growth at this stage resembling a mulberry. The pedicle becomes wider and shorter until in time it is as wide as the growth itself which is no longer pedunculated but sessile. The surface has now lost its bright clean appearance and is covered with phosphates and pus; later still it becomes necrotic. At the same time infiltration takes place at the base, and oedema, often of the bullous type, can be observed in the adjacent mucosa, whilst there may be more generalized cystitis. The growth has now become a papillary carcinoma. (*See* Fig. 44.)

Diffuse papillomatosis

At any time during this process seedling growths may appear elsewhere in the bladder and undergo similar changes. Vesical papilloma is credited with the ability to produce implants by detached surface cells; contact growths are found in the areas where the walls of the empty bladder are opposed. (*See* Fig. 45.) Disturbance of the growth during open operation is in a similar way sometimes followed by widespread dissemination within the bladder or in the abdominal wall. This is less often seen after closed cystoscopic diathermy. Diffuse spread, whether originating in the bladder or in the renal pelvis or ureter, may however be due to an inherent tendency to papillomatosis independent of contact or implantation.

Large benign papilloma

In exceptional cases papillomas may reach a large size, almost filling the bladder without showing any of the changes described.

Spread beyond the bladder is rare, but in a case which has become malignant lymphatic dissemination may occur.

(ii) *Nodular carcinoma.*—Whereas the villous papilloma is tufted, the surface of a nodular carcinoma is bald from the outset. It appears as a smooth nodule of growth, red in colour and less pedunculated than a papilloma; as it grows it

becomes lobulated. Its surface is soon covered with purulent debris and phosphates and becomes necrotic. (*See* Fig. 46.) Microscopically it is a transitional-celled carcinoma and infiltrates the bladder wall; glandular metastases may be found. Local spread may lead to fixity to surrounding structures. In malignancy it is intermediate between papillary and ulcerating carcinoma.

(iii) *Ulcerating carcinoma.*—Malignant ulceration is similar to that seen elsewhere. The ulcer has an irregular outline, its edge is raised and its base composed of necrotic new growth. It infiltrates the bladder deeply and adheres to the pelvic wall. Glandular metastases may become widespread, involving not only the pelvic and aortic glands, but also those of the mediastinum and neck. Less commonly there are deposits in the lungs, liver or bones. This is the most malignant form of bladder cancer.

Character of ulcer

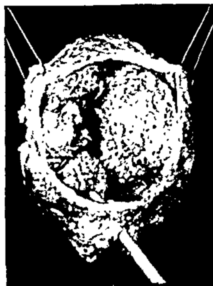


Fig. 45.—Diffuse papillomatosis which has become carcinomatous. Total cystectomy specimen.

Macalpine (1936) suggests that the ulcerating type of carcinoma is formed by necrosis of the surface mass of a nodular tumour. This does occur, but there is also a primary ulcerating type; the discovery of a small epitheliomatous ulcer is evidence in this direction.

(iv) *Adenocarcinoma.*—There is a group of apical tumours whose structure is that of an adenocarcinoma with extensive colloid degeneration. Histologically they are indistinguishable from a carcinoma of the rectum, and their origin has been attributed to an inclusion of primitive hindgut, but Begg (1931) considers that they arise from remnants of the urachus. Macroscopically they resemble the nodular carcinoma. They spread upwards along the urachus, and give rise to metastases in the abdominal wall or within the abdomen.

Theories of origin

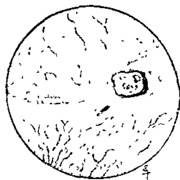


Fig. 46.—Nodular carcinoma near the left ureteric orifice.

Polygonal-cell tumours suggesting a glandular origin sometimes arise in the bladder base.

(v) *Endometrioma.* — Vesical endometriosis may have a connexion with the uterine mucosa, or more rarely be quite separate from it (Weijtlandt, 1934). It gives rise to an acinar tumour lined with cylindrical epithelium. This forms a vascular projection behind the trigone which shares in the uterine engorgement of menstruation, when it bleeds.

(b) Secondary tumours

Renal and ureteric

(i) *Spreading from other parts of the urinary tract.*—The primary tumour may be a papilloma or papillary carcinoma of the renal pelvis or ureter spreading by cellular implantation; tumours at the ureteric orifice should always be suspect of a renal origin, as should those which recur quickly after treatment. The bladder tumours in such cases are usually benign papillomata, but if left they undergo malignant changes; they are often multiple.

Prostatic

Carcinoma of the prostate spreads into the bladder, producing oedema of the base; it may also form secondary isolated nodules of growth, particularly in the region of the ureteric orifices.

Tumours may arise in diverticula; from their proximity to the pelvic wall they soon become adherent.

Uterine

(ii) *Extensions from extra-urinary sources.*—Carcinoma of the uterus invades the bladder by direct extension. It produces an elevation of the posterior vesical wall which later fungates. Eventually a vesico-vaginal fistula may result from a cervical growth.

Rectal and colonic

Carcinoma of the rectum or sigmoid colon may adhere to and invade the bladder. It gives rise to a localized area of cystitis at the site of adhesion, which in the case of the sigmoid is typically above the left ureteric orifice. Inflammation becomes intense at this point and a fistula forms, first gas, then pus, and finally faeces escaping into the bladder; by this time growth can usually be seen in the bladder mucosa.

5. MORBID ANATOMY

Cystitis

Other pathological changes produced in the urinary tract are due to infection and obstruction. A benign tumour is not usually accompanied by cystitis, but infection may supervene on repeated cystoscopic treatment, or if it becomes malignant.

Hydronephrosis

Obstructive changes depend upon the site of the tumour; when situated at the internal meatus it will give rise to hypertrophy, then dilatation of the bladder and dilatation of the ureters and renal pelves. A growth at a ureteric orifice will cause unilateral hydronephrosis and hydro-ureter. (*See* Fig. 48.)

6. CLINICAL PICTURE

Haematuria

The outstanding clinical manifestation of any bladder tumour is haematuria; it is the first sign in more than 80 per cent of cases, and often remains the only sign for a long period.

(1) Benign tumours

The bleeding of a papilloma has certain well-defined characteristics. Its onset is sudden; it is profuse, producing "total haematuria" sometimes with clots, and is painless. After a few hours or days it ceases spontaneously. Even without treatment there may be no further bleeding for months or years until another unprovoked attack occurs. Each succeeding haemorrhage becomes more copious and prolonged. The adage that profuse, painless, periodic haematuria is diagnostic of papilloma of the bladder is very often true.

Dysuria

When papillomas become multiple or large they may arouse a feeling of

incomplete emptying, with increased frequency. A tumour *overlying the* internal meatus may cause difficulty in micturition or an intermittent stream.

Abdominal, rectal and vaginal examination are negative; the urine, even in the absence of blood, may contain a little albumin.

(2) Malignant tumours

The initial signs of a malignant tumour are identical with those of a benign papilloma, but bleeding is more persistent, and *the early onset of cystitis* causes dysuria with scalding or pain on micturition. Intense referred pain may follow adhesion to the pelvic wall, but as a rule pain is only connected with micturition apart from a dull suprapubic ache. In a late stage painful strangury may be intolerable. Renal pain indicates ureteric obstruction.

A malignant tumour is sometimes palpable per abdomen or on bimanual pelvic and abdominal examination. Enlarged glands may be felt, and in the latest stages there may be clinical and radiological signs of metastases in the lungs or in bones, and evidence of cachexia and anaemia from repeated haemorrhage.

Special symptoms

Special types of growth may alter the clinical picture. Pain is earlier in an ulcerating carcinoma. An endometrioma may produce regular monthly bleeding. A sarcoma in an infant sometimes causes retention of urine. Secondary growths generally give evidence of their primary situation before vesical symptoms appear.

7. SPECIAL AIDS TO DIAGNOSIS

(1) Cystoscopy

The bladder occupies a unique position amongst the body cavities in the facility with which it can be examined precisely. It can be washed out and distended, and a tumour can be examined from a distance and in close detail.

Necessity for cystoscopy

Cystoscopy is indicated in every case of haematuria, and unless there are special contra-indications, such as severe infection or anaemia, it should be the first investigation after the clinical examination of the patient and of the urine. The fact that haematuria has ceased does not absolve the surgeon from this duty.

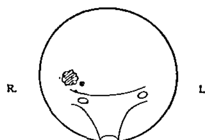


FIG. 47.—Cystoscopic record of bladder tumours.

The first object is to find the source of the bleeding, the second the nature of the lesion producing it. A patient seen when bleeding should be cystoscoped at that time. This can be done with an examination cystoscope under local anaesthesia, and a positive diagnosis can be made in most cases. If there is no lesion in the bladder or urethra it can be seen whether the bleeding comes from one or both kidneys. A record should be made at the time. (*See* Fig. 47.)

In a few cases a complete diagnosis cannot be made at this preliminary cystoscopy. The conditions making for difficulty are:

Difficulties

(a) A small urethra. Meatotomy or dilatation may be needed before a cystoscope can be introduced.

(b) Severe haemorrhage. If the bleeding is copious it may be impossible to get the medium sufficiently clear for accurate diagnosis.



Fig. 48.—Large nodular carcinoma at left ureteric orifice with hydro-ureter. Excretion cystogram showing filling defect in the bladder.

(c) Infection. With some malignant tumours cystitis may make the bladder intolerant and reduce its capacity to an extent incompatible with precise observation.

(d) Extensive growths. In cases in which the tumour almost fills the bladder it may be impossible to say more than that a growth is present.

Cystoscopy under anaesthesia

In any of these circumstances it is advisable to admit the patient and repeat the examination under an anaesthetic. A low spinal, combined if desired with intravenous anaesthesia, is suitable. It allows of urethral dilatation, the introduction of a larger cystoscope of the constantly irrigating type, and gives sufficient relaxation for the bladder to be filled.

Removal of clot

If clots obscure the picture they may be liquefied by the instillation of glycerin of pepsin (1 fluid ounce retained for 15–20 minutes), followed by aspiration and repeated lavage. This method is preferable to the use of an evacuator which may cause more haemorrhage.

Blood transfusion

If anaemia is severe blood transfusion is necessary before cystoscopy.

The difficulties are rarely insuperable, and the value of accurate cystoscopic diagnosis is so great that no effort should be spared to achieve it. Diagnostic cystotomy introduces the danger of dissemination; the suprapubic scar detracts from subsequent operative exposure and makes planned treatment more difficult.



Fig. 49.—Large papilloma of bladder base causing urethral obstruction. There is also a diverticulum but the bladder is otherwise regular.

(2) Biopsy

Limitations of biopsy

A piece of growth can be removed with a cystoscopic rongeur for histological examination. Its value is doubtful, for unless part of the base can be removed, no evidence of infiltration is obtained. To the experienced eye the cystoscopic appearance of a tumour gives more accurate information about its nature than does a cystoscopic biopsy.

(3) Radiography

An x-ray examination will sometimes reveal phosphatic incrustation on a tumour and will distinguish it from a vesical calculus.

Excretion urography is useful in demonstrating kidney function; it also affords an incidental cystogram, and although the shadow is not dense it often demonstrates a filling defect caused by the growth. (*See* Fig. 48.) A cystogram, made by filling the bladder with opaque medium (sodium iodide, 10 per cent solution), shows greater contrast and gives some indication of the extent of large or multiple tumours. Benign tumours show an irregular outline in a bladder which is otherwise regular and of good capacity. (*See* Fig. 49.) Malignant tumours have a more sharply defined margin, but when there is infiltration the bladder outline is irregular, its capacity diminished, and its shape altered. *Excretion urography* *Cystography*

Air cystography is also used. All such investigations are useful adjuncts to cystoscopy.

8. DIFFERENTIAL DIAGNOSIS

Other causes of haematuria must be considered.

Urethral bleeding is bright red and occurs independently of micturition. A urethral caruncle in the female can be seen; papilloma in the male is discovered on urethroscopy. *Haematuria*

Vaginal or uterine bleeding in the female must be excluded by examination, and, if doubt exists, by cystoscopy.

Renal new growth is the other common lesion causing symptomless haematuria; cystoscopy during bleeding shows blood coming from the ureter. In polycystic kidneys or medical causes it may come from both ureters.

Apart from such rare conditions as varix and bilharzia, and the commoner one of enlarged prostate, other causes of vesical bleeding are stone and cystitis. A stone covered with debris may simulate a growth encrusted with phosphates but the former can be moved whilst the latter bleeds when touched with a ureteric catheter; x-ray examination will settle the diagnosis.

With dysuria as the main symptom, the diagnosis between growth and cystitis may not be easy; in some forms of cystitis there are hypertrophic changes producing polypoid masses resembling a tumour, but with a more translucent appearance. *Cystitis*

The diagnosis between a papilloma and a frank carcinoma presents no difficulties, but doubt may be felt over a papillary growth showing some signs of malignancy. Purulent exudate and stunted villi may still leave it more benign than malignant, but a broad pedicle and surrounding oedema suggest infiltration and it should be treated as malignant. In a doubtful case it is correct to apply diathermy and re-examine in four weeks, warning the patient that open operation may become necessary. During the treatment the electrode can be withdrawn slightly whilst the current is on to test for mobility. Such a therapeutic test is justifiable and may save a major operation. *Doubtful growths* *Therapeutic test*

9. PROGNOSIS

All bladder tumours will destroy life if untreated. The simple papilloma either becomes malignant or causes death from exsanguination; growth, however, is slow.

Causes of death

Infection and obstruction, with pyelonephritis and uraemia are more frequent causes of death than is haemorrhage.

10. CHOICE OF TREATMENT

The methods available are surgery and irradiation, or both combined, and judgement in selection is of equal importance to skill in application. The choice depends upon the nature, size, multiplicity and site of the growth, and the general condition of the patient.

(1) Surgery

The general indications are:

1. (a) Closed (cystoscopic). Coagulation-diathermy. Papillomas of small or moderate size.

(b) Open (through cystotomy). Large or multiple papillomas.

(c) Chemical coagulation with trichloracetic acid has also been used for large papillomas.

2. Excision. Localized papillary or nodular carcinomas.

3. Partial cystectomy. Larger nodular or ulcerating carcinomas, and urachal growths.

4. Total cystectomy. Diffuse papillomatosis, extensive papillary or nodular carcinoma, especially basal, and possibly endometrioma.

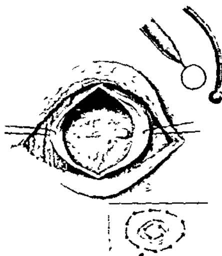


Fig. 50.—Implantation of radon seeds. Inset below shows the scheme of distribution. Insets above shows the electrodes for removal of the surface growth and light coagulation of the base.

(2) Irradiation

1. X-ray therapy. Sarcomas, diffuse vascular tumours or inoperable growths.

2. Radium needles or radon seeds. Sessile infiltrating but localized growths.

The radio-sensitivity of bladder tumours is not high, but irradiation will sometimes stop bleeding. The direct application of x-rays to a growth through a cystotomy opening by the Chaoul applicator is still on trial but offers a more accurate method of restricting the irradiation to the affected area.

Cystoscopic implantation of radon seeds has a limited application, but their insertion by open operation gives greater possibility of uniform irradiation. (*See* Fig. 50.)

(3) Combined methods

For multiple papillary carcinomas where the age or general condition of the patient precludes total cystectomy x-ray treatment may be combined with cystodiathermy. Diathermy should not be given until a month after x-ray

treatment or severe cystitis will result. Radium needles may also give rise to localized cystitis or ulceration.

Inoperable growths are not always alleviated by x-ray treatment; strangury may be helped by suprapubic cystotomy, but deviation of the urine by ureteric transplantation is better. Pre-sacral sympathectomy sometimes relieves pain, provided that the disease is still confined to the bladder. *Palliative treatment*

11. PRE-OPERATIVE MANAGEMENT

The most important pre-operative measure is to impress upon the patient the need for regular attendance for follow-up cystoscopy. *Follow-up cystoscopy*

Before cystoscopic treatment of papillomas no special measures are required. With larger growths it is wise to determine the renal function by blood-urea estimation and intravenous urography. *Renal function*

Sepsis, unless severe, may be neglected before an open operation as the bladder will be drained afterwards; with serious infection intermittent lavage with silver nitrate solution 1 : 5,000, may help, and sulphonamides should be given. *Sepsis*

Blood transfusion is indicated in exsanguinated cases, and in all cases a high fluid intake should be maintained. *Blood transfusion*

Before total cystectomy the ureters are transplanted into the colon or to the skin. In the former case the bowel must be prepared by aperients, lavage and succinylsulphathiazole (Sulphasuxidine) 60 grammes over 4 days. *Intestinal antiseptics*

12. OPERATIVE TECHNIQUE

Diathermy is used in almost all bladder operations; the padded indifferent electrode should be placed on the thigh, and no metal must touch the skin or a burn will result. *Use of diathermy*

(1) Coagulation diathermy

(*a*) *Cystodiathermy*

For any but the smallest papillomas an irrigating cystoscope is a great advantage; the field can be kept clear and a larger active electrode (size 9 Ch.) used. Small satellite growths are destroyed first lest they be obscured later. The electrode is placed on the tumour and a weak current turned on by the foot-switch, the aim being to produce coagulation, not charring. The whole tumour is treated with no attempt to sever the pedicle unless all the surface has been coagulated. The electrode is withdrawn when necessary to clean off coagulated tissue which interferes with conductivity. Treatment stops when coagulation is complete, or the medium can no longer be kept clear. The bladder is then washed out with silver nitrate solution (1 : 5,000) and 2 fluid ounces left in. *Satellite tumours*

For large papillomas Kidd's cystoscope (*see* Fig. 51) is quicker and more efficient. *Larger papillomas*

For small papillomas a local anaesthetic suffices if a small cystoscope is used, but full anaesthesia is preferable.

For tumours near the internal meatus a retrograde telescope is helpful but a prostatic electrotome is better.

(b) Open diathermy

The bladder is filled with silver nitrate solution 1 : 5,000. In a moderate Trendelenburg position a transverse or vertical subumbilical incision is made

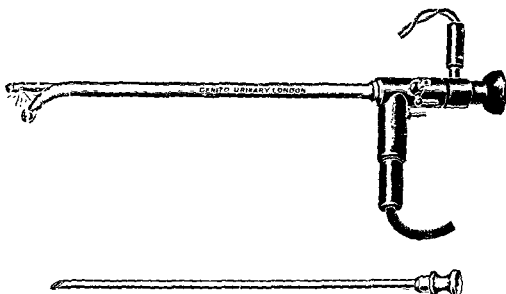


FIG. 51.—Kidd's cystoscope.

Avoidance of leakage

and the recti are separated. (*See* Fig. 52.) The peritoneum is stripped up, the bladder fixed by two hooks and emptied by a trocar and cannula attached to a sucker. (*See* Figs. 53 and 54.) It is opened and a self-retaining retractor is inserted. The tumour is handled as little as possible; it is coagulated with a ball or disc electrode (*see* Fig. 50) until destroyed. The bladder is irrigated with silver nitrate solution 1 : 5,000 and closed around a drainage tube brought out through the top of the bladder and the middle of the abdominal incision. A pre-vesical drain is inserted. (*See* Figs. 55 and 56.)

Site of drainage high

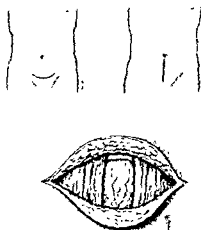


FIG. 52.—Exposure of the bladder. Insets show alternative skin incisions.

(2) Excision

The bladder is opened as before and the surface of the tumour coagulated. It is excised with half an inch of surrounding mucosa with a diathermy needle. (Fig. 54.) After attention to haemostasis the bladder is repaired by a continuous suture of fine, plain catgut and closed with drainage. (*See* Fig. 57.)

(3) Partial cystectomy

Mobilization

The bladder is mobilized, particularly in the region of the tumour, before it is emptied. If the tumour is in the fundus the peritoneum may be opened and

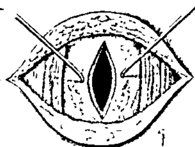


FIG. 53.—The bladder opened after being emptied by trocar and cannula.

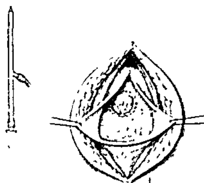


FIG. 54.—Excision of tumour. The trocar and cannula attached to a sucker are used for the preliminary emptying.

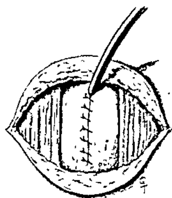


FIG. 55.—The bladder closed with the drainage catheter emerging from the upper end of the incision.



FIG. 56.—The recti closed with drainage. If a transverse skin incision is used the catheter is brought out through a separate stab wound above it.



FIG. 57.—Closure of the bladder in the same case as Fig. 54.



FIG. 58.—Re-implantation of the ureter after excision of a tumour near it. (*After Grey Turner.*)

any adherent part excised with the tumour. The bladder is then opened and the growth, with half an inch of healthy tissue around it, is excised by diathermy with the whole thickness of the bladder wall. If this area includes the ureter its cut end must be re-implanted into the bladder at a convenient part of the incision. This may be done by one of two methods:

Re-implantation of ureter



FIG. 59.—Re-implantation of the ureter; the drainage tube passes into the extravesical tissues. (*After Grey Turner.*)

(a) The ureter is fixed by two catgut stitches to the lips of the bladder incision; a small drainage tube is stitched beside it, reaching the extravesical tissues, crossing the bladder, and emerging from the wound. It is left for 10 days and resulting scar tissue keeps the ureteric orifice open. (*See* Figs. 58 and 59.)

(b) The ureter is split vertically on each side for a quarter of an inch; the two flaps are sutured inside the bladder. (*See* Fig. 60.) The defect in the bladder is repaired by two rows of catgut sutures inserted from outside. Drainage is provided for the bladder and the extravesical region, the tubes emerging from the middle of the incision.

Urachal tumours

In an apical adenocarcinoma Begg recommends that the urachus and umbilicus should be removed with the upper half of the bladder.

(4) Total cystectomy

Deviation of the urine

This is preceded by transplantation of the ureters into the colon or to the skin. Cutaneous ureterostomy gives less liability to renal infection but involves a permanent double urinary fistula; uretero-intestinal anastomosis is preferable.

Simultaneous bilateral ureteric transplantation reduces the operations from three to two, but often causes disturbance of the renal excretory mechanism with signs of uraemia. Unilateral transplantations at two weeks' interval are freer from this risk.

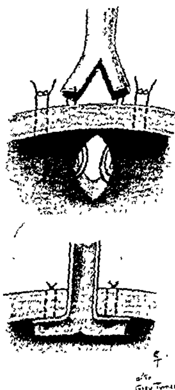


FIG. 60.—Re-implantation of the ureter: alternative method. (*After Grey Turner.*)

The right ureter is transplanted first. An oblique incision is made in the right inguinal region. The muscles are divided and the peritoneum is retracted. The ureter is found posteriorly, adhering to the parietal peritoneum; it is followed into the pelvis, divided, and the lower stump ligated. The peritoneum is

opened longitudinally for four inches behind the spermatic vessels; the lowest loop of pelvic colon or the caecum is withdrawn through the peritoneal incision and sutured to its edges. (*See* Fig. 61(a).) The rest of the operation is extraperitoneal.

Extraperitonealization of the bowel

The bowel is incised for one and a half inches through its peritoneal and muscle coats, which are dissected back. (*See* Fig. 61(b).) The ureter is brought into this bed, and its length adjusted so that it lies without tension or looping; a piece of its lower end can usually be sacrificed with advantage. The ureter is cut obliquely and a double-needled suture of chromic catgut tied through the tip. A stab opening is made into the colon at the lower end of the prepared bed and the ureteric sutures are passed through it to emerge outside the bowel half an inch lower, where they are tied.

Fixation of the ureter

The muscle flaps of the colon are joined over the ureter by interrupted sutures and invaginated by a continuous suture; there must be no compression of the ureter and no tension. (*See* Fig. 61(c).) The anastomosis is dusted with a sulphonamide powder and the wound closed with drainage.

Completion of anastomosis

Isotonic sodium sulphate (3·3 per cent) is given by intravenous drip, and a rectal tube is inserted.

After two weeks the left ureter is similarly transplanted through a left inguinal incision.

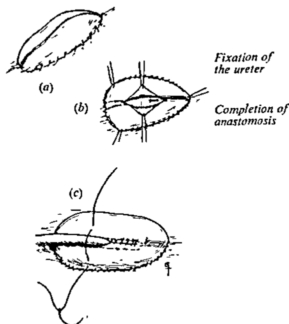


FIG. 61.—Transplantation of the ureter into the colon. (*a*) Knuckle of colon stitched outside the peritoneum. (*b*) Muscular coats incised and reflected (*c*) Suture of the bowel over the ureter. (*After Grey Turner.*)

Technique of cystectomy

Three weeks later the bladder is removed. It is filled with silver nitrate solution 1 : 1,000 through a tied-in rubber catheter. In full Trendelenburg position the abdomen is opened through a median subumbilical incision. The peritoneum is stripped from the dome and posterior wall of the bladder, the urachus being divided. The superior vesical vessels are reached and divided, and mobilization from above is carried down to the inferior vesical vessels. (*See* Fig. 62.) The bladder is now emptied through the catheter.

At the lower end the pubo-prostatic ligaments are cut, and the urethra is divided by diathermy at the apex of the prostate; the catheter acts as a guide and is cut by curved scissors. The prostate is seized with a vulsellum and separated from the rectum from below upwards; a hot swab controls venous bleeding. Upward traction is made on the prostate whilst the seminal vesicles are separated from the rectum. (*See* Fig. 63.) At their apex a vascular pedicle including the vas is secured and separation proceeds until the inferior vesical vessels are tied. These pedicles are then tied on the opposite side and the bladder is removed.

In the female the line of separation is between the bladder and the anterior vaginal wall.

Bleeding points are secured; bleeding from around the cut urethra is best controlled by diathermic coagulation.

Drainage The cut end of the catheter is drawn into the pelvis and anchored as a

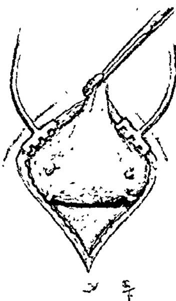


FIG. 62.—Total cystectomy. The urachus and the superior vesical vessels have been divided.

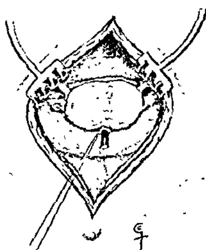


FIG. 63.—Total cystectomy; the prostate and seminal vesicles are removed from below upwards.

drain; it should be removed in the male after two days owing to the danger of urethritis.

The cavity is well coated with a sulphonamide powder and abdominal drainage provided.

Rectal tube The rectal tube is replaced for a few days.

13. POST-OPERATIVE CARE

After all bladder operations a high fluid intake must be maintained. Sulphonamides are best reserved until needed.

Closed operations After cystodiathermy the patient is discharged about the third day, but is warned of the possibility of slight secondary haemorrhage about the tenth. He returns for cystoscopy in four weeks; earlier than this all the coagulated mass may not have separated, but by this time the need for further treatment can be assessed.

Open operations After open operations the bladder should be washed out and the suprapubic tube retained until the urine is clinically clean.

14. RESULTS OF TREATMENT

Cysto-diathermy The results of cystodiathermy for benign papilloma are excellent in early cases. Small tumours can be destroyed at one session; larger ones require

repeated treatment, but it is always better to do the maximum at the first sitting with adequate anaesthesia than frequent short sessions under local anaesthesia; repeated instrumentation favours infection.

Partial cystectomy

Partial cystectomy gives good results in selected cases. There is some danger of disseminating the growth by manipulation. If more than a third of the bladder is removed the viscus will be left with a small capacity; some dilatation occurs in course of time, but where the growth is large it is better to do a total cystectomy than an extensive partial cystectomy.

Transplantation of ureters

The immediate results of transplantation of the ureters are good and the operative mortality is low. Although there is inevitably some renal infection and dilatation, both subside as a rule, and the patient can hold urine in the rectum for four or more hours and often throughout the night.

Total cystectomy

The operation of total cystectomy is a more formidable procedure, especially in cases on the borderline of operability. It is hardly worth undertaking for ulcerating carcinoma in which lymphatic metastases are not infrequent, nor in any case where the growth is fixed, except as a palliative procedure. Such cases develop early recurrence, but escape the painful strangury of advanced carcinoma of the bladder.

It would appear that the results of treatment can be improved in two ways:

1. By the insistence on cystoscopy in all cases of haematuria.
2. By recognizing that extensive papillary tumours are probably already malignant and should be treated radically by total cystectomy.

Figs. 59, 60 and 61 are modified from the article on the Kidney and Ureter by John Everidge in Grey Turner's *Modern Operative Surgery*.

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[References to other titles are given under Bladder—Tumours in the Index Volume. The subject of Neoplasms is also dealt with under the heading of Bladder Diseases in the *British Encyclopaedia of Medical Practice* (1936), Vol. 2, p. 374.]

BLINDNESS–MANAGEMENT OF

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GENERAL

59.] As the subject of management of blindness at all age levels is too wide for this article, only the earlier stages in adults catastrophically blinded by injury and accident will be considered, and in these the emotional and social factors rather than the ophthalmological or surgical.

Removal of blind eyes

Unless both eyeballs have been absolutely destroyed there is no call for removal of both damaged eyes, even though hopelessly injured and without perception of light. The emotional support from the possession of "an eye", though sightless and for which no hope has been given, may be considerable. Only later, pain or gross unsightliness should call for removal of the eye, and the surgeon should approach this irretrievable step carefully.

(1) Emotional and social factors

Telling the patient

As soon as the patient inquires about his prospects for sight the issue must be faced honestly and thoroughly. In the seriously ill man it may be well to evade finality, but evasions must be carefully made, for even in the early stages anxiety and fear will make the man very suspicious. If the eye condition makes ultimate decision as yet impossible the position must be thoroughly explained, but when blindness is certain to result, and the man is fit to be told and is able to accept the position, he must be told.

Emotional reactions

As in any serious loss, the emotional reactions vary widely—anger, depression, and defiance in varying type and degree. Commonly enough, anger with "fate" is "worked out" by irritability and annoyance with those around, and must be met with tolerance and, later, reasoned firmness. No "slap on the back" cheeriness will help the profoundly depressed; kindness and patience may be severely taxed in helping the newly blind. Many may talk of the further uselessness of living and suggest suicide, but in only a small proportion is the emotional disturbance grossly uncontrolled, although watch should be kept so long as suspicions are not aroused.

(2) Rehabilitation

Personal habits and early rehabilitation

To help and support the man, physical and social aid can supplement the more definitely spiritual. He should be encouraged to do as much as he can for himself as early as is possible; to put his things—his cigarettes, his ash-tray, his clothes and so forth—in regular order; to feed himself, at first with spoon and deep plate, and later with knife and fork from an ordinary plate; to dress and shave himself. He needs his letters read to him, and this must be done quite impersonally. He will appreciate reading of the daily paper and

of books, to supplement the wireless, which is so great a help to the blind. He must not be hurried, or allowed to drift; he must have plenty of time for sleep and rest, and he may require sedatives at night. Often he will smoke too much, and may try the line of drowning his sorrows. All these issues require watching and common-sense handling. The more subtle psychological reactions—the turning of night into day, the natural turn to human support which so often calls for female company and sex activity in the male, and the later psychological twists—may all be seen, but only infrequently need special handling. As soon as is possible the man should be encouraged to walk and get about his room, his house and his garden. He should be helped only to the degree of giving him initial confidence and in order to avoid accidents. To help him, objects should always be in the same place; a fall over a chair left about, or a bump into a perambulator or motor-car outside the door may set back growing confidence to quite an extraordinary degree. Doors should be shut and never left ajar; the man will very soon feel for, and find, the handle to let himself in and out. When entering his room the visitor should announce himself, talk naturally to him and not shout, and announce his departure. The blind man should never be touched without first warning him, and any happening of which he is unaware because of his blindness should be announced, to allay unnecessary suspicion about what may be going on. Appointments and promises should be strictly kept, and he should never be allowed to think he is a burden or unwanted, useless. He is very soon and very naturally envious of the sighted; he has inner conflict over his self-esteem, and he has lost his sense of personal inviolability, and is fearful and suspicious of all around him. Everything done for him should be done in the light of these effects of blindness. The slowing down of everything, the bumps, and the anxieties, readily produce grumbling and irritability which should be disregarded as far as is possible.

(3) The future and its approach

The future

The newly-blind patient has early and natural anxiety about his future, especially about his family and their support, and in all this he needs assurance that provision for him and for them will be forthcoming, that he will not be unacceptable to them and the world, and that later many forms of employment, bringing in wages and also restoring his self-esteem, are available. If possible, a Braille watch made especially for the blind should be obtained. Time passes slowly and the satisfaction of being able to feel the time by day or night, as soon as is possible, is of great value. If it can be obtained, paper with raised ridges as lines will help him to write letters, but if a typewriter is available anybody who can use it can quickly teach him touch-typing on a standard machine. The joy and "uplift" of being able to send letters, and the pleasure of making progress, are extremely helpful. Many simple things for him to do can help a lot—making string bags on a frame, plaiting string, simple weaving and rug making, on frame or canvas—leading up to more skilled occupations, killing time, bringing interest and sharpening touch and the senses. In the early stages he may well require dark glasses for comfort, and the use of these is commonly continued, partly to mask disfigurement, and partly for psychological reasons. While best discarded as soon as possible many a man feels that dark glasses and a white stick give him help in public, where his disability may be

overlooked, and the aid he needs be quite unwittingly withheld. The provision of artificial eyes when possible is perhaps best left until the man enquires about them. Their use marks the loss of hope of vision, which many like to postpone. Braille training should be arranged whenever possible, either by a home teacher or, better still, in a communal life, for in spite of the recognized undesirability of segregating the disabled, a spell of community life definitely does help to ease difficulties, and to tide many a man over the earlier stages of acute envy against the sighted world. Later still, training for suitable employment should be arranged when possible, and this, naturally, demands some degree of community life in a training centre.

Notification of blindness

For all these measures, the aid of a local or National Blind Organization should be sought, notification of the blinded person's state having been made as early as is possible.

[References to other titles are given under Blindness—Management of in the Index Volume.]

BLOOD AND BLOOD-FORMING ORGANS: BLOOD EXAMINATION

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overlooked, and the aid he needs be quite unwittingly withheld. The provision of artificial eyes when possible is perhaps best left until the man enquires about them. Their use marks the loss of hope of vision, which many like to postpone. Braille training should be arranged whenever possible, either by a home teacher or, better still, in a communal life, for in spite of the recognized undesirability of segregating the disabled, a spell of community life definitely does help to ease difficulties, and to tide many a man over the earlier stages of acute envy against the sighted world. Later still, training for suitable employment should be arranged when possible, and this, naturally, demands some degree of community life in a training centre.

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In foetal life haemopoiesis also occurs in the haemopoietic cells of the reticulo-endothelial system throughout the tissues, the formation leaving the organs other than marrow, spleen and lymph glands as full-term approaches. Such haemopoietic activity may recur during adult life giving rise to "myeloid transformation", that is to say active proliferation of blood-forming tissue in response (a) to increased calls for blood cells such as occurs in the haemolytic anaemias or (b) in response to unknown stimuli such as occur in the various hyperplastic conditions of haemopoietic tissues known under the wide collective name of the "reticuloses". With suitable stimulation the pluri-potent reticulum cells of the reticulo-endothelial system may give rise to proliferation of any or all of the more specialized cell types. Such proliferation may lead to enlargement of the organs most affected, as of the spleen in haemolytic anaemias or both spleen and liver in certain reticuloses and leukaemias. *(b) foetal*

2. THE FUNCTION OF THE BLOOD-FORMING ORGANS

The function of the haemopoietic tissue in the blood-forming organs is to supply formed elements for the circulating blood but this tissue is also found in organs with other functions. Only diseases affecting the haemopoietic tissue in the blood-forming organs are discussed here.

(1) *The spleen*

Apart from its potentialities as an organ of haemopoiesis the spleen clearly is concerned to some extent in red cell destruction. It is found to be enlarged in chronic haemolytic anaemias and its removal checks, if it does not completely end, the abnormal haemolytic process. How far this process is an exaggeration of its normal action is not known. There is much discussion as to whether the fundamental abnormality in acholuric jaundice is due to changes in the red cell or in the spleen (Dacie, 1943). Experimental work on the effects of splenectomy in animals should be regarded with suspicion since the spleen in certain animals, at least, holds a haemolytic organism, Bartonella, in check; the results of splenectomy are, therefore, often complicated by the sudden activity of a Bartonella infection. It has been suggested that the spleen exerts a regulating effect on the erythropoietic activity of the bone marrow (Singer, Miller and Dameshek, 1941; Jacobson and Williams, 1945). This awaits confirmation.

(2) *The liver*

The liver is indirectly concerned in erythropoiesis since it is the source of certain haemopoietic factors. How far it acts as a storehouse for principles used elsewhere in the body and how far it is essential to their metabolism is not clear. Furthermore, it is probably concerned in the metabolism of haemoglobin (Rimington, 1939b; Watson, 1942). Disorders of the liver are likely, therefore, to be associated with abnormal erythropoiesis.

(3) The bone marrow

In healthy adult life the bone marrow is the only source of mature cells of the myeloid series. Active marrow is found in the upper one-third of the femur and humerus and in the flat bones such as the sternum and pelvis. The rest of the marrow is fatty. Considerable

1. DEFINITION OF THE BLOOD AND BLOOD-FORMING ORGANS

60.] The peripheral blood and the blood-forming tissue may be regarded as a single organ, one or more parts of which may be affected by changes of a physiological or pathological nature.

Composition of the blood

The circulating blood carries in the plasma mature red and white blood cells and platelets. The origin of the cells of the blood and the character of their precursors is still disputed, but the fundamental observations of Maximow and his co-workers (1927), which have not been disproved, form a useful basis for classification. The white cells are of three types arising from three different precursors, namely: the myeloid type; neutrophil polymorphonuclear cells, eosinophil polymorphonuclear cells, basophil polymorphonuclear cells; the lymphoid type, the lymphocytes; and the monocytic type, the monocytes. In adult life the red cells, the white cells of the myeloid type and the platelets are formed by the haemopoietic cells of the reticulo-endothelial system in the bone marrow. White cells of the lymphoid type originate from the reticulum cells of lymph follicles in the spleen and lymph glands; white cells of the monocytic type arise from sinus reticulum.

Origin of cells of the blood (a) adult

4,870 cubic centimetres, the difference between the sexes being due largely to the greater red cell volume of the male (Gibson and Evans, 1937).

(2A) Haemoglobin

Haemoglobin is expressed below in terms of the National Physical Laboratory comparator as standardized by the British Standards Institute and the National Physical Laboratory for the following reasons.

(1) Instruments for use with this scale are available and are standardized by the National Physical Laboratory (B.S.I. 1079). All observers can work to the same scale and in due course will be able to convert their results into grammes per cent of haemoglobin.

(2) There are difficulties at the moment in expressing haemoglobin in terms of oxygen capacity or iron content (Macfarlane and his colleagues, 1944). Attractive though it is to express haemoglobin in grammes per cent, the fundamental basis for doing so is not, at present, sound, and an arbitrary colour standard is preferable. Results so obtained, it is hoped, will be able to be converted into grammes per cent in due course (Macfarlane and his colleagues, 1944; Medical Research Council *Special Report Series*, No. 252, 1945).

(*a*) *Men*

The mean haemoglobin level for men is 105 per cent (N.P.L. Standard) with a range of from 90·669 per cent to 123·291 per cent (Price-Jones, Vaughan and Goddard, 1935).

(*b*) *Women*

The mean haemoglobin level for women is usually accepted as being in the neighbourhood of 98·2 per cent. There is evidence that given an adequate iron intake this might be raised to 103·1 (Yudkin, 1944).

(*c*) *Infants*

No satisfactory normal haemoglobin figures are available for infants and young children in Great Britain, since the majority of observations have been made on children in a poor social class in which conditions could not be considered optimal (Medical Research Council *Special Report Series*, No. 252, 1945).

(*d*) *The mean corpuscular haemoglobin concentration* (*M.C.H.C.*)

This figure expresses the relationship between haemoglobin saturation and cell volume. The degree of saturation is expressed by stating the haemoglobin content in grammes per cent as a percentage of the cell volume in cubic centimetres. *Mean corpuscular haemoglobin*

$$\frac{\text{Haemoglobin in grammes per 100 c.cm. of blood} \times 100}{\text{Volume of packed red cells in c.cm. per 100 c.cm. of blood}}$$

The difficulty in using this figure at the moment lies in the fact that haemoglobin cannot be accurately expressed in grammes. Using American figures which probably will correspond closely to English figures the normal range is 33–38 per cent. For purposes of calculation of M.C.H.C. 100 per cent haemoglobin (N.P.L. standard) should be taken as 14·7 grammes of haemoglobin (Macfarlane and his colleagues, 1944).

active haemopoiesis. With increased demands for myeloid cells active haemopoiesis may spread throughout the skeleton.

(4) The lymph glands

In normal circumstances the lymph glands are the source of mature lymphocytes. Their other functions are not for discussion in this article. Myeloid transformation may occur in pathological conditions in which there is an abnormal demand for myeloid cells, or an abnormal stimulation and proliferation occurs as in certain reticuloses.

3. THE FUNCTION OF THE BLOOD

Carrier

The blood is a passive carrier which comes into contact with all the tissues, transporting, as well as the formed elements, the complex chemical substances required by the tissues. The term "diseases of the blood", however, usually is taken to cover only abnormalities in these formed elements or in the clotting mechanism which is dependent upon the interaction of factors in the vessels, the plasma and the structural elements. It does not include abnormalities in the chemical structure of the plasma except in so far as this may affect the clotting mechanism.

Cellular abnormalities

Abnormalities in the circulating cells of the haemopoietic organs may be of two types as follows. (1) The abnormality may be the response to a physiological or pathological process in some other part of the body as, for example, the leucocytosis which occurs in infections, or the megalocytic anaemia associated with carcinoma of the stomach. (2) The abnormality may be symptomatic of a physiological or pathological process in one or other parts of the haemopoietic organ—as, for example, the occurrence of abnormal myeloid cells in myelogenous leukaemia. An examination of the circulating blood picture and, in appropriate instances, of the characteristics of haemopoietic tissue by sternal puncture or gland biopsy, therefore, will inevitably throw light upon a wide variety of clinical conditions.

4. NORMAL VALUES

Red cell counts and haemoglobin levels are so influenced by many variable factors, particularly different elements in the diet, that it is difficult to give any reliable figures for normal. Furthermore, methods of estimating haemoglobin are at the moment far from satisfactory. The following figures should be regarded as those usually seen in an average cross section of the English population, rather than a true normal. They are in reasonable agreement with figures from the United States of America. The figures for men are probably more satisfactory than are those for women (Medical Research Council *Special Report Series*, No. 252, 1945).

(1) Blood volume

Average figures

Estimations of blood volume owing to technical difficulties are open to question. The average figure recorded for 49 males in one series, in whom estimations were made by the Evans blue technique, was 5,335 cubic centimetres—the range was from 3,610 to 6,980 cubic centimetres. The average figure for 41 females was 3,800 cubic centimetres—the range was from 3,030 to

Bergh reaction is not necessarily a measure of haemolysis but rather of liver efficiency. The only certain measure of increased extravascular haemolysis is the estimation of the amount of urobilinogen excreted in the faeces. Cases of acholuric jaundice, for instance, may show a normal indirect van den Bergh reaction, but also a greatly increased excretion of urobilinogen. Such patients if they have an attack of hepatitis may show an approximately unaltered excretion of pigment but a high indirect van den Bergh reaction.

In the case of intravascular haemolysis some of the liberated haemoglobin may be excreted as such in the urine where it is converted into methaemoglobin and acid haematin. Some is broken down in the blood stream to haematin and globin. The haematin links with plasma albumin to form methaemalbumin, which is unable to pass through the glomeruli of the kidney and probably is broken down in the liver and excreted in another form (Rimington, 1939; Fairly, 1941). Methaemalbumin gives the plasma a peculiar mahogany colour. It can be detected by Schumm's test. It has been suggested that intracorpuscular degradation of haemoglobin also occurs (Watson, 1942). *Haemoglobin breakdown to methaemalbumin*

(3) Total red cell count

(a) Men

5,422,000 per cubic millimetre with a range from 4,530,000 per cubic millimetre to 6,310,000 per cubic millimetre (Price-Jones, Vaughan and Goddard, 1935). *Average counts*

(b) Women

5,012,000 per cubic millimetre with a range from 3,940,000 per cubic millimetre to 6,080,000 per cubic millimetre.

(c) Infants

At birth the figure may be as high as 7,000,000 per cubic millimetre, falling to a figure of 5,000,000–5,500,000 in twelve days (Whitby and Hynes, 1935). Other observers give rather lower figures.

(d) The mean corpuscular volume (M.C.V.)

This figure expresses the mean or average volume of a single red cell in cubic microns (cμ). The normal range is 78–94cμ. Anything outside this range is microcytic or macrocytic. *Mean corpuscular volume*

(4) Plasma bilirubin

The level of plasma bilirubin giving the indirect van den Bergh reaction in 100 healthy adults ranged from 0·2–1·7 milligrams per 100 cubic centimetres, 93 per cent of values being below 0·8 milligram per 100 cubic centimetres. The mean value for the series was 0·539 milligram per 100 cubic centimetres (Vaughan and Haslewood, 1938). *Plasma bilirubin*

(5) Sedimentation rate

The sedimentation rate expresses the rate at which the red cells sediment on standing so long as the tubes are kept vertical and the temperature reasonably constant. This rate depends upon the number of red cells and the character of the plasma. In order to obviate the effect of anaemia a correction must be introduced. The test is non-specific but is extremely valuable.

Broadly speaking, an abnormal sedimentation rate is found (a) in the presence of infection, (b) when there is destruction of tissue or (c) disturbance of the *Interpretation*

(2B) Haemoglobin metabolism

(a) *Haemoglobin synthesis*

The exact steps in the synthesis of haemoglobin are complex (Rimington, 1936 and 1939b; Watson, 1938); they are not for discussion in this article. It must be remembered, however, that a complete study of pigment excretion, covering urobilinogen and the porphyrins both in urine and in faeces, is required in order to throw light on the mechanism of anaemia production in a wide variety of conditions. Few anaemias, for instance, can be classified as haemolytic unless such studies are made (Vaughan and Saifi, 1939).

(b) *Haemoglobin breakdown*

Red cell breakdown

The normal mechanism of red cell destruction is unknown. The accepted explanation is that the cells undergo fragmentation as the result of the physical stresses to which they are subjected in the circulation (Rous, 1923), the fragments being removed by cells of the reticulo-endothelial system, a large portion of which is located in the spleen. Haemoglobin breakdown normally is considered to be extravascular. It has been said that whereas it is unknown whether or not the spleen is the slaughter-house of the red cell there is a general consensus of opinion that it does serve as its graveyard (Davis, 1944).

Extravascular haemolysis

Intravascular haemolysis

In certain circumstances intravascular haemolysis with intravascular breakdown of haemoglobin occurs in the plasma. This is known to take place in mismatched transfusions and in certain heterospecific pregnancies when a recognizable haemolysin is present (*see* page 215). It is also characteristic of blackwater fever. Maegraith and his colleagues, (1943a, 1943b) describe the presence in various human tissues of a haemolytic agent the action of which is inhibited by a factor present in normal serum. They suggest, therefore, that normal haemolysis may be governed by a balance between the lytic agent and the serum inhibitor. Reduction in the latter, they believe, occurs in blackwater fever, and is responsible for the excessive haemolysis.

Haemoglobin breakdown to urobilinogen

The van den Bergh reaction

The fate of pigment released by extravascular and intravascular haemolysis is different. In the case of normal extravascular haemolysis, haemoglobin is converted by a series of steps into bilirubin. This passes back into the blood stream when it unites in some way with albumin and passes to the liver (Watson, 1938 and 1942). In the liver, the union with albumin is broken down and the bilirubin is excreted into the bile and then passes into the intestinal canal when it is excreted as urobilinogen. If there is obstruction to the excretion of bile, the bilirubin is reabsorbed and appears in the plasma no longer bound to albumin. In its free form bilirubin reacts directly with a diazo reagent giving rise to the immediate positive van den Bergh reaction. Such a reaction is only positive in the presence of obstruction to bile excretion. When bound to albumin before passing through the liver, bilirubin gives no direct reaction with a diazo reagent and is only detected after the addition of alcohol which breaks down the union with albumin. Plasma, which reacts with a diazo reagent only after addition of alcohol, is said to give an indirect van den Bergh reaction. Normal plasma may contain small amounts of such bilirubin (*see* page 165). If the liver is efficient large quantities of bilirubin may be rapidly removed from the plasma. If the liver is inefficient even the normal removal may not take place so that the level of the indirect van den-

Direct van den Bergh reaction

Indirect van den Bergh reaction

the physiological stimulation of high altitudes only occurs in polycythaemia vera.

(*a*) *Polycythaemia vera*

Polycythaemia vera, or "erythroleukaemia" or Vaquez-Osler's disease, is, as far as is at present known, a primary disease of erythropoietic tissue characterized by splenomegaly, a raised total red cell count, and sometimes a raised total white cell count with abnormal cells present in the peripheral blood. The diagnosis should not present difficulties; surgical intervention is not called for. *Polycythaemia vera*

(*b*) *Anaemia*

Anaemia may be caused by three essentially different mechanisms which form the basis of a classification. *Anaemia*

(1) The dyshaemopoietic anaemias due to failure or abnormality in blood production. *Classification of anaemias*

(2) The post-haemorrhagic anaemias due to abnormal loss of blood.

(3) The haemolytic anaemias due to excessive destruction of blood *in vivo*.

(4) There is a further small group whose aetiology is obscure, which may be called the unclassified anaemias.

6. THE ANAEMIAS

(1) Dyshaemopoietic anaemias

(*a*) *The deficiency anaemias*

A large group of anaemias is due to a deficiency of one or more of the factors required for erythropoiesis.

The known factors essential for erythropoiesis.—The known essential erythropoietic factors are (i) a group of substances present in liver, some of which at least are closely associated with the vitamin B complex; (ii) iron and possibly traces of other minerals particularly copper and possibly cobalt and manganese; (iii) vitamin C; (iv) thyroxine; (v) certain amino acids particularly lysine and methionine. *Liver* *Iron* *Vitamin C* *Thyroxine* *Amino acids*

The effective principles in liver are complex and their relationship is at present obscure (Spies and his colleagues, 1945; Watson and Castle, 1945; Davidson, 1945; Vilter, Spies and Koch, 1945). There are probably small differences in the type of blood picture produced by a deficiency of one or other but the general characteristics are the same and serve to distinguish them as a group from the majority of other anaemias. *Effective principles in liver*

Mechanism of deficiency production.—A deficiency of essential haemopoietic factors may be brought about in a variety of ways.

(i) a lack of normal factors in the diet as in nutritional macrocytic anaemia. *Diet*

(ii) an increased demand for one or more factors, as in pregnancy. *Increased demands*

(iii) deficient digestion so converting an adequate food intake into an inadequate one. *Digestion*

(iv) deficient absorption converting an adequate diet into an inadequate one. *Absorption*

(v) deficient metabolism of digested and absorbed haemopoietic principles such as occurs in cirrhosis of the liver. *Metabolism*

Morphological characteristics of deficiency anaemias.—The blood picture produced by iron deficiency is characteristic. The total red cell count is not necessarily affected, but there is a marked reduction in haemoglobin. In *Iron deficiency*

protein content of the plasma. Changes in the sedimentation rate in a patient with a chronic infection, such as tuberculosis, are of value in prognosis and in assessing the value of treatment. The finding of a high sedimentation rate in a patient with no physical signs should always arouse suspicion, whereas a normal sedimentation rate in a patient with many symptoms but no localizing signs suggests that there is no cause for anxiety. The normal range in men is 0 to 9 millimetres and for women 0 to 15 millimetres at the end of one hour.

Normal levels

(6) Total white cell count

The limits of a normal leucocyte count are from 4,000 to 10,000 per cubic millimetre. As a rule no significance can be attached to fluctuations of less than 50 per cent in the total count, and 10 per cent in the differential count.

(7) Differential white cell count

Differential leucocyte count

A differential count expressed as a percentage is misleading. It should be expressed in absolute figures. The normal range is shown below.

Neutrophil polymorphonuclears	3,000 to 6,000 per cubic millimetre
Eosinophil polymorphonuclears	150 to 400 per cubic millimetre
Basophil polymorphonuclears	0 to 100 per cubic millimetre
Lymphocytes	1,500 to 2,700 per cubic millimetre
Monocytes	350 to 500 per cubic millimetre

(8) Platelets

Platelets

The normal platelet count may vary from 250,000 to 500,000 per cubic millimetre.

5. DISORDERS OF THE BLOOD AND BLOOD-FORMING ORGANS

Space does not permit of detailed analysis of the diseases of the blood and blood-forming organs. Certain general principles only are discussed in this article and special emphasis is laid on points of surgical interest.

(1) Blood volume

Reduction

A decrease in circulating blood volume occurs characteristically as the result of blood loss due to injury and after burns. In the latter it is, at least in part, dependent upon plasma lost from the burnt area and into the surrounding tissues. It occurs also in severe chronic anaemias (Sharpey-Schafer, 1945) when it is presumably a compensatory mechanism enabling what little haemoglobin is left to be circulated more rapidly. This reduction must be remembered in the transfusion of patients with long-standing anaemias. Such patients should be given frequent small transfusions of concentrated red cells at an extremely slow rate.

Relation to transfusion

An increase in blood volume is known to occur in patients with an arterio-venous fistula, polycythaemia and pneumococcal pneumonia; such patients should not receive transfusions, since overloading the circulation is a serious risk.

(2) Disorders of erythropoiesis

The commonest disorders of erythropoiesis result in anaemia due to a fall in either red cells or haemoglobin, or in both. An excess of red cells apart from

with haemoglobin (Plate IV (*a*)) (Vaughan, 1938). When first seen the blood picture may appear simple, but after treatment with the necessary haemopoietic factor the blood picture may change and become characteristic of lack of another factor (Vaughan, 1932). Finding a dimorphic picture in patients on a reasonable diet should always suggest a gastro-intestinal lesion. A similar blood picture is often seen in African natives in whom there is probably a complex aetiology, namely long-standing multiple dietary-deficiency and intestinal lesions (Trowell, 1942).

Gastric carcinoma

There is some connexion between gastric carcinoma and Addisonian pernicious anaemia (Duehring and Eusterman, 1942) though its nature is not clear. In a series of 293 patients with pernicious anaemia on whom a necropsy was performed 12·3 per cent were found to have gastric carcinoma as compared with an incidence of 4 per cent among a large group of other cases of similar ages (Kaplan and Rigler, 1945; Olson and Heck, 1945). It has been suggested that all patients with known Addisonian pernicious anaemia should receive a bi-annual x-ray examination in order to detect the development of any growth. Certainly the diagnosis of Addisonian pernicious anaemia should not be made without radiological examination of the gastro-intestinal canal.

Other gastric lesions

Megalocytic hyperchromic anaemias responding to liver treatment are also recorded following complete gastrectomy (Farris, Ransom and Coller, 1943), partial gastrectomy (Singer, Miller and Dameshek, 1934), gastro-enterostomy (Singer, Miller and Dameshek, 1934; Larsen, 1934); gastro-colic fistula (Fairley and Kilner, 1931), intestinal obstruction due to tuberculous stricture (Meulengracht, 1929) and in patients with multiple anastomoses following appendicitis (Little, Zerfas and Truster, 1929). Such lesions may, however, be without effect upon the blood picture (Jones, 1940).

Gastro-enterostomy

From a practical point of view it is particularly important to watch the blood picture in patients with a gastro-enterostomy. In such patients mild degrees of anaemia are far more common than is generally recognized and may account for much malaise. A haemoglobin below 80 per cent well merits treatment. The anaemia in such patients is due probably to hurry in the small intestine resulting in inadequate absorption of haemopoietic principles (Hartfall, 1934) and to the bland diet often prescribed for the gastric patient. It is essential to secure a good diet rich in haemopoietic factors for all patients after gastro-intestinal operations. A six-monthly blood examination is indicated. Any deficiency which appears should be treated with adequate dosage of the required haemopoietic factor (Jones, 1940).

Bacterial synthesis in intestines

Recent experimental work suggests that synthesis of certain components of the vitamin B complex by intestinal bacteria may prove of considerable importance in erythropoiesis (Nielsen and Elvehjem, 1942; Wilson and his colleagues, 1942; Axelrod and his colleagues, 1943). Intestinal lesions may, therefore, affect haemopoiesis by their influence on intestinal flora, and possibly by their effect on the production of aromatic hydrocarbons which may in certain conditions affect haemopoiesis (Bomford and Rhoads, 1941).

(*b*) *Treatment of deficiency anaemias*

The essential factor in treating the deficiency anaemias is to give an adequate dosage of the missing factor or factors.

Iron

Iron must be given by mouth. Many patients respond well to 9 grains of ferrous sulphate daily, but there is a large group who require at least double

stained films the red cells are small and contain little haemoglobin; it is par excellence an hypochromic microcytic anaemia (Plate III (*a*)). The picture produced by a deficiency of the effective principles in liver is also characteristic. There is a greater reduction in total red cells than in haemoglobin and the mean size of the red cells is increased though there is great variation in size, and often in shape. It is a hyperchromic megalocytic anaemia (Plate III (*b*)). In certain circumstances discussed below a dual deficiency may exist giving a mixed picture sometimes spoken of as dimorphic anaemia (Plate IV (*a*)).

Liver-principle deficiency

The anaemia associated with both vitamin C deficiency and thyroid deficiency may be either hyperchromic and megalocytic or hypochromic and microcytic. The diagnosis cannot be made from the blood picture alone.

Vitamin C
Thyroid

Relationship of the gastro-intestinal canal to anaemia.—It is clear from the above analysis of the mechanism of erythropoietic factor deficiency production that disturbances of gastro-intestinal function, however produced, may well affect erythropoiesis (Vaughan, 1938). The discovery of an unexplained anaemia should always direct attention to the gastro-intestinal canal.

Gastro-intestinal function

There is often a combination of one or more of the factors above. Dietary deficiencies as well as causing a lack of some essential factor may also impair digestion. For instance, the megalocytic hyperchromic anaemia often associated with pellagra is due probably to a long-standing deficiency of Castle's extrinsic factor in the diet, associated with poor intestinal absorption and, in some cases, defective excretion of the intrinsic factor (Moore and his colleagues, 1944). The interpretation of the part played by deficient digestion in disturbances of erythropoiesis though recognized as of great importance is, at the moment, extremely confused. It is becoming increasingly difficult to reconcile the many experimental and clinical results recorded.

Pellagra

Gastric digestion

It is generally agreed that iron is better absorbed from an acid than from an alkaline medium. Anything causing a decrease in hydrochloric acid excretion will, therefore, interfere with absorption of iron and favour the development of an iron deficiency anaemia.

Hydrochloric acid

Thus the development of iron deficiency anaemia is seen associated with complete gastrectomy and partial gastrectomy, with gastro-enterostomy, with intestinal obstruction and with gastric carcinoma.

The original experiments of Castle and his colleagues suggested that the development of Addisonian pernicious anaemia was dependent upon a failure on the part of the stomach to secrete "intrinsic factor" which reacted with "extrinsic factor" present in the diet to form the effective principle in liver commonly spoken of as the pernicious anaemia principle. This interpretation of certain experimental work has admittedly been a valuable working hypothesis but may need some modification in the future (Jones, 1940; Jacobson and his colleagues, 1945; Spies and his colleagues, 1945; Vilter, Spies and Koch, 1945). Gastric secretion, apart from hydrochloric acid, is concerned in the formation of essential haemopoietic factors, but exactly how it plays a part and to what extent this part is essential must be regarded as uncertain.

Pernicious anaemia principle
Intrinsic factor
Extrinsic factor

A common characteristic of anaemias associated with structural lesions of the gastro-intestinal canal other than Addisonian pernicious anaemia is that they are often, though not invariably, dimorphic, that is, there is a deficiency of iron, causing the production of small pale red-cells, and a deficiency of one or more of the principles in liver, causing production of large cells well filled

Dimorphic anaemia

with haemoglobin (Plate IV (a)) (Vaughan, 1938). When first seen the blood picture may appear simple, but after treatment with the necessary haemopoietic factor the blood picture may change and become characteristic of lack of another factor (Vaughan, 1932). Finding a dimorphic picture in patients on a reasonable diet should always suggest a gastro-intestinal lesion. A similar blood picture is often seen in African natives in whom there is probably a complex aetiology, namely long-standing multiple dietary-deficiency and intestinal lesions (Trowell, 1942).

Gastric carcinoma

There is some connexion between gastric carcinoma and Addisonian pernicious anaemia (Duehring and Eusterman, 1942) though its nature is not clear. In a series of 293 patients with pernicious anaemia on whom a necropsy was performed 12·3 per cent were found to have gastric carcinoma as compared with an incidence of 4 per cent among a large group of other cases of similar ages (Kaplan and Rigler, 1945; Olson and Heck, 1945). It has been suggested that all patients with known Addisonian pernicious anaemia should receive a bi-annual x-ray examination in order to detect the development of any growth. Certainly the diagnosis of Addisonian pernicious anaemia should not be made without radiological examination of the gastro-intestinal canal. Megalocytic hyperchromic anaemias responding to liver treatment are also recorded following complete gastrectomy (Farris, Ransom and Coller, 1943), partial gastrectomy (Singer, Miller and Dameshek, 1934), gastro-enterostomy (Singer, Miller and Dameshek, 1934; Larsen, 1934); gastro-colic fistula (Fairley and Kilner, 1931), intestinal obstruction due to tuberculous stricture (Meulengracht, 1929) and in patients with multiple anastomoses following appendicitis (Little, Zerfas and Truster, 1929). Such lesions may, however, be without effect upon the blood picture (Jones, 1940).

Other gastric lesions

Gastro-enterostomy

From a practical point of view it is particularly important to watch the blood picture in patients with a gastro-enterostomy. In such patients mild degrees of anaemia are far more common than is generally recognized and may account for much malaise. A haemoglobin below 80 per cent well merits treatment. The anaemia in such patients is due probably to hurry in the small intestine resulting in inadequate absorption of haemopoietic principles (Hartfall, 1934) and to the bland diet often prescribed for the gastric patient. It is essential to secure a good diet rich in haemopoietic factors for all patients after gastro-intestinal operations. A six-monthly blood examination is indicated. Any deficiency which appears should be treated with adequate dosage of the required haemopoietic factor (Jones, 1940).

Bacterial synthesis in intestines

Recent experimental work suggests that synthesis of certain components of the vitamin B complex by intestinal bacteria may prove of considerable importance in erythropoiesis (Nielsen and Elvehjem, 1942; Wilson and his colleagues, 1942; Axelrod and his colleagues, 1943). Intestinal lesions may, therefore, affect haemopoiesis by their influence on intestinal flora, and possibly by their effect on the production of aromatic hydrocarbons which may in certain conditions affect haemopoiesis (Bomford and Rhoads, 1941).

(b) *Treatment of deficiency anaemias*

The essential factor in treating the deficiency anaemias is to give an adequate dosage of the missing factor or factors.

Iron

Iron must be given by mouth. Many patients respond well to 9 grains of ferrous sulphate daily, but there is a large group who require at least double

this dose, and others who do far better on *iron and ammonium citrate* 90 grains daily. If iron causes diarrhoea a bismuth mixture should be given; if it causes constipation liquid paraffin usually is helpful. Hydrochloric acid may be given in addition but is not essential. A follow-up of women with iron deficiency anaemia almost always shows that the anaemia recurs unless treatment is maintained. In the case of the megalocytic hyperchromic anaemias, if the aetiology is in doubt, it is best to give a crude liver extract like Campolon or Hepastab by injection, or proteolysed liver extract by mouth (Davidson, 1945), rather than the highly purified extracts like Anahaemin. There are apparently refractory cases of megalocytic hyperchromic anaemia of various types that respond to oral treatment only (Watson and Castle, 1945). Anahaemin is effective in Addisonian pernicious anaemia but is not always of use in other forms of megalocytic hyperchromic anaemia such as tropical nutritional anaemia and sprue (Davis and Davidson, 1944). In the future, it is probable that folic acid will be available for the treatment of this group of anaemias by mouth (Spies and his colleagues, 1945; Vilter, Spies and Koch, 1945). It is essential to keep the red cell count at 5,000,000 per cubic millimetre and the haemoglobin at 100 per cent. If iron is given as well in some cases there is no reason why such a result should not be achieved.

Liver extracts

Dosage

Initial treatment should be intensive. If laboratory facilities are available the success of treatment may be judged by daily reticulocyte counts (Minot and Castle, 1935), otherwise a steady rise in haemoglobin and total red cell count must be used as a guide to treatment. Maintenance treatment should be given at not longer than monthly intervals, the dose required being worked out by a process of trial and error for each patient. Although it is theoretically possible to give a bigger depot dose it is wiser to see the patient frequently as, in the presence of a passing infection, it is often necessary to increase the dosage.

Thyroid

The anaemias associated with thyroid deficiency are often complex and may require treatment with either liver or iron as well as thyroid (Bomford, 1938).

Vitamin C

The anaemia of scurvy responds to adequate dosage with vitamin C.

(*c*) *The metabolic anaemias*

It has, in recent years, become increasingly apparent that certain anaemias, previously regarded as haemolytic or aplastic, are dependent upon some generalized disturbance of metabolism.

(*d*) *Factors concerned*

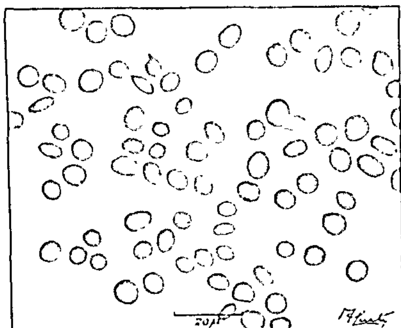
Characteristics

(i) *Chronic infection.*—Chronic infective processes are associated almost invariably with some degree of anaemia. This anaemia usually affects both red cells and haemoglobin, and it fails to respond to either liver or iron (Vaughan and Saifi, 1939; Saifi and Vaughan, 1944). It appears probable that the anaemia is due to some interference with haemoglobin synthesis (Vaughan and Saifi, 1939) depending upon abnormalities in iron utilization induced by the inflammatory process. There is no evidence of marrow aplasia or of increased haemolysis. At the moment transfusion is the only recognized line of treatment. A high protein, high vitamin diet should be ensured.

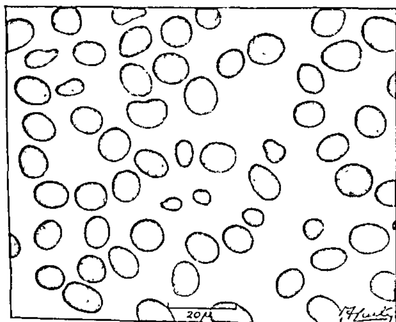
Cause

(ii) *Trauma.*—Experience in the last six years has shown that varying degrees of anaemia develop after injury however slight. A simple fracture of the patella is sufficient to cause a fall in red cells and haemoglobin (Vaughan, 1945). The fall in haemoglobin is associated with a fall in protein, particularly

Associated metabolic abnormalities



(*a*) Red cells from a case of simple iron deficiency. Note the small poorly stained red cells. (Jenner stain.)



(*b*) Red cells from a moderately severe case of Addisonian pernicious anaemia. Note the anisocytosis, poikilocytosis, polychromasia and megalocytosis. (Jenner stain.)

PLATE III

affecting the albumin fraction (Vaughan, 1945), and a greatly increased nitrogen excretion (Taylor and his colleagues, 1943; Cuthbertson, 1944). The interaction between these metabolic disturbances is not yet clear. The increased nitrogen excretion cannot be entirely prevented by giving a high protein diet (Stevenson, 1945), but there is evidence that it is reduced by a high calorie, high protein diet. A diet of 3,500–4,000 calories containing 150-180 grammes of protein was used successfully in the later months of the war. This was obtained by adding well-flavoured milk shakes containing dried egg to the ordinary ward diet. *Dietary treatment*

If necessary the anaemia should also be treated with repeated blood transfusions. This is particularly important in the case of severe burns when, in addition to the metabolic factor, increased haemolysis due to injury of the red cells at the time of burning (Shen, Ham and Flemming, 1943) is also operative. It is essential in treating injured patients to remember that this anaemia is likely to develop. If they have to be given intravenous fluids, blood should be given as well as glucose-saline. *Transfusion*

(iii) *Diseases of the liver.*—Anaemia is often associated with diseases of the liver (Vaughan, 1936). In some instances it can be attributed to lack of the pernicious anaemia factor (Goldhamer and his colleagues, 1934). In others it may well be due to disturbances in protein metabolism affecting haemoglobin synthesis. The possible part played by different amino acids particularly lysine (Harris, Neuberger and Sanger, 1943) and methionine (Glynn, Himsworth and Neuberger, 1945) in haemopoiesis is likely to be of considerable significance. The aetiology of certain obscure anaemias may prove to be associated with a deficiency of certain specific amino acids. *Protein metabolism*

Many of the anaemias hitherto regarded as haemolytic probably are due, at least in part, to disturbances of haemoglobin metabolism dependent upon some form of liver disorder as suggested particularly in regard to the anaemias associated with chemical poisons. *Relation to haemolytic anaemias*

(iv) *Anaemia associated with nephritis.*—The morphological character of the anaemia in nephritis is similar to that seen in trauma and sepsis. There is also no diminution in marrow activity. It appears likely that the cause of this anaemia will be found on investigation to be a disturbance of haemoglobin metabolism. The possibility of renal disease as a cause of unexplained anaemia, especially in a man, must be remembered. *Nephritis*

(e) *Toxic anaemias*

(i) *Due to irradiation.*—Internal irradiation with radio-active substances, such as occurs in dial painters using radio-active paint, may result in a megalocytic hyperchromic anaemia associated with necrosis of bones or, in the late cases, sarcomatosis (Martland, 1931). External irradiation from radium and various forms of x-rays is likely to affect the white cells, especially the lymphocytes, more than the red cells. Both anaemia and polycythaemia have been described in persons so exposed (Rolleston, 1930). *Radio-active substances*

(ii) *Due to chemical poisons.*—The action of a large group of chemical substances on haemopoiesis is extraordinarily complex as pigment studies have shown. Many of the arsenical compounds, lead, the sulphonamides and phenylhydrazine certainly have, at least, a dual action. The sulphonamides interfere with haemoglobin formation (1) by affecting the synthesis of essential factors by intestinal bacteria (Axelrod and his colleagues, 1943; Daft and *Arsenicals* *Sulphonamides*

Sebrell, 1943; Carter and his colleagues, 1945); (2) by giving rise to liver dysfunction (Watson and Spink, 1940); and (3) by disturbing the normal breakdown of haemoglobin (Rimington, 1939a). They also cause haemolysis of varying degree (Watson and Spink, 1940). Lead probably interferes with the synthesis of haemoglobin (Rimington, 1939). A further group of refractory anaemias due to the toxic action of aromatic hydrocarbons, of either exogenous or endogenous origin, is recognized in which analysis of pigment metabolism has shown that haemolysis and disordered liver function both play a part (Bomford and Rhoads, 1941). *Phenylhydrazine* Phenylhydrazine, which causes haemolysis, has long been known also to injure the liver and, therefore, has a dual effect on haemopoiesis.

(f) Unexplained dyshaemopoietic anaemia

(i) *Aplastic anaemia.*—Profound anaemia is occasionally found in association with complete aplasia of the marrow. *Marrow aplasia* The diagnosis can be made only at necropsy after examination of the whole skeleton. The cause is unknown. Transfusions must be given as often as are required.

(ii) *Leuco-erythroblastic anaemia.*—Anaemia, often mild in degree, characterized by the presence in the peripheral blood of extremely young red cells and white cells, without a leucocytosis, is associated with a variety of conditions affecting the bones. The discovery of this blood picture should always suggest an examination of the skeleton. It may indicate the presence of an unsuspected carcinoma with secondary deposits in the bone (Vaughan, 1938). *Carcinomatosis* It is found in the following: carcinomatosis, myelomatosis, myelosclerosis, *Bone disease* Cooley's anaemia or Mediterranean fever, marble bone disease of Albers-Schönberg and in Hodgkin's disease with secondary deposits in the marrow. If a normal blood picture is present it does not rule out the possibility of marrow deposits in a patient with malignant disease but a leuco-erythroblastic blood picture always means skeletal involvement. There is no treatment, except in myelosclerosis in which transfusions are unexpectedly successful in relieving the anaemia temporarily.

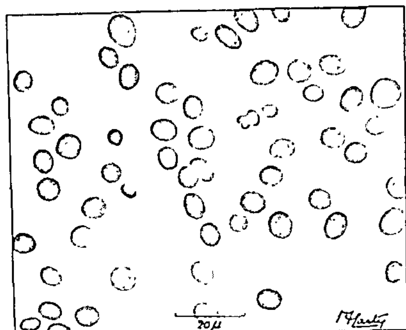
(2) The post-haemorrhagic anaemias

Characteristics The anaemia due to simple blood loss of an acute type shows an equal reduction in red cells and in haemoglobin. If the loss be of long standing it may have led to a depletion of the body's store of iron and the anaemia will then be microcytic and hypochromic in type.

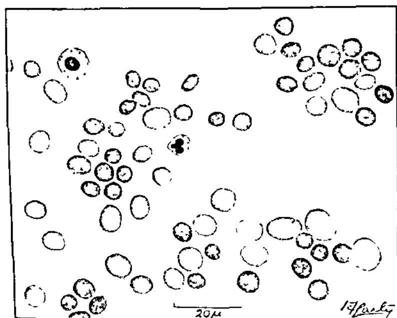
A severe microcytic hypochromic anaemia in a man should lead to a search for a possible source of blood loss from an unsuspected gastric or duodenal *Haemorrhoids* ulcer or from haemorrhoids. In sudden severe haemorrhage the picture may be leuco-erythroblastic in type. In a woman, it should be remembered that *Menorrhagia* menorrhagia is far more commonly dependent on the anaemia than vice versa. Unless fibroids or other gross pathological changes are present in the uterus, hysterectomy should not be performed until adequate iron therapy has been given. In the initial period of treatment the haemorrhage may become worse but equilibrium is usually established within six months.

(3) The haemolytic anaemias

No anaemia should be regarded as haemolytic unless there is unimpeachable *Diagnostic features* evidence of increased haemolysis such as the presence of methaemalbumin in the peripheral blood stream, haemoglobin pigments in the urine or



(*a*) Red cells from a case of dimorphic anaemia associated with gastro-intestinal disturbance. Note variation in density of red cell staining and in red cell size. (Jenner stain.)



(*b*) Red cells from a case of haemolytic anaemia. Note the dense-looking microcytes, the polychromasia and the normoblasts, one with a moniliform distortion of the nucleus. (Jenner stain.)

PLATE IV

Sebrell, 1943; Carter and his colleagues, 1945); (2) by giving rise to liver dysfunction (Watson and Spink, 1940); and (3) by disturbing the normal breakdown of haemoglobin (Rimington, 1939a). They also cause haemolysis of varying degree (Watson and Spink, 1940). Lead probably interferes with the synthesis of haemoglobin (Rimington, 1939). A further group of refractory anaemias due to the toxic action of aromatic hydrocarbons, of either exogenous or endogenous origin, is recognized in which analysis of pigment metabolism has shown that haemolysis and disordered liver function both play a part (Bomford and Rhoads, 1941). Phenylhydrazine, which causes haemolysis, has long been known also to injure the liver and, therefore, has a dual effect on haemopoiesis.

Phenyl-hydrazine

(*f*) *Unexplained dyshaemopoietic anaemia*

(i) *Aplastic anaemia.*—Profound anaemia is occasionally found in association with complete aplasia of the marrow. The diagnosis can be made only at necropsy after examination of the whole skeleton. The cause is unknown. Transfusions must be given as often as are required.

Marrow aplasia

(ii) *Leuco-erythroblastic anaemia.*—Anaemia, often mild in degree, characterized by the presence in the peripheral blood of extremely young red cells and white cells, without a leucocytosis, is associated with a variety of conditions affecting the bones. The discovery of this blood picture should always suggest an examination of the skeleton. It may indicate the presence of an unsuspected carcinoma with secondary deposits in the bone (Vaughan, 1938). It is found in the following: carcinomatosis, myelomatosis, myelosclerosis, Cooley's anaemia or Mediterranean fever, marble bone disease of Albers-Schönberg and in Hodgkin's disease with secondary deposits in the marrow. If a normal blood picture is present it does not rule out the possibility of marrow deposits in a patient with malignant disease but a leuco-erythroblastic blood picture always means skeletal involvement. There is no treatment, except in myelosclerosis in which transfusions are unexpectedly successful in relieving the anaemia temporarily.

Carcinomatosis

Bone disease

(2) The post-haemorrhagic anaemias

Characteristics

The anaemia due to simple blood loss of an acute type shows an equal reduction in red cells and in haemoglobin. If the loss be of long standing it may have led to a depletion of the body's store of iron and the anaemia will then be microcytic and hypochromic in type.

A severe microcytic hypochromic anaemia in a man should lead to a search for a possible source of blood loss from an unsuspected gastric or duodenal ulcer or from haemorrhoids. In sudden severe haemorrhage the picture may be leuco-erythroblastic in type. In a woman, it should be remembered that menorrhagia is far more commonly dependent on the anaemia than vice versa. Unless fibroids or other gross pathological changes are present in the uterus, hysterectomy should not be performed until adequate iron therapy has been given. In the initial period of treatment the haemorrhage may become worse but equilibrium is usually established within six months.

Haemorrhoids

Menorrhagia

(3) The haemolytic anaemias

No anaemia should be regarded as haemolytic unless there is unimpeachable evidence of increased haemolysis such as the presence of methaemalbumin in the peripheral blood stream, haemoglobin pigments in the urine or

Diagnostic features

increased excretion of urobilinogen in the faeces. A raised plasma bilirubin may be dependent upon disordered liver function rather than increased haemolysis. When liver function is efficient plasma bilirubin may be normal though haemolysis is present. Other features of haemolytic anaemias, which, however, alone cannot be regarded as diagnostic are: the colour index is usually in the neighbourhood of unity; the reticulocyte count is raised; and young red and young white cells are present in the peripheral blood stream. Stained films show spherocytosis and microcytosis or megalocytosis (Plate IV (*b*)). The fragility of the red cells in normal saline is usually increased.

Splenomegaly

Chronic haemolytic anaemias are associated with splenomegaly and occasionally with enlargement of the liver. Enlargement of the spleen is not found in acute haemolytic anaemias unless haemolysis is extremely severe.

The haemolytic anaemias can be roughly grouped according to their aetiology. Analysis of the pigment metabolism, however, in the case of anaemias due to chemical substances shows that the mechanism of anaemia production is rarely simple.

Classification

(a) Those due to an extrinsic agent, namely malaria, *Bacillus welchii*, oroya fever, favism, chemical poisons.

(b) Those due to an abnormality of the red cells, namely sickle cell anaemia, acholuric jaundice (Dacie and Mollison, 1943) and nocturnal haemoglobinuria (Scott, Robb-Smith and Scowen, 1938; Ham, 1939).

(c) Those due to an abnormal haemolysin, namely paroxysmal cold haemoglobinuria, some cases of acute haemolytic anaemia, mismatched transfusions (*see* page 215), haemolytic disease of the new-born (*see* page 213).

(d) Unexplained haemolytic anaemias.

Chemical agents which may cause haemolysis in susceptible individuals are benzene and arseniuretted hydrogen. Probably they also affect haemoglobin metabolism but pigment studies are not available.

Splenectomy

Splenectomy in chronic malaria, for mechanical reasons, is sometimes performed, the large spleen being an encumbrance; the results are rarely satisfactory. Splenectomy is not indicated in other haemolytic anaemias due to extrinsic agents, nor in those due to an abnormal haemolysin. The results of splenectomy in sickle cell anaemia are disappointing. The possibility however of the sickle cell trait as the fundamental disease process should always be remembered in negroes. Neither anaemia nor splenomegaly is necessarily present and the characteristic sickling of the cells may be missed. The symptomatology is protean. Many cases present as an acute abdomen and unnecessary laparotomies are performed. Bone and joint symptoms are common (Bauer and Fisher, 1943). In acholuric jaundice as in sickle cell anaemia the symptoms are extremely varied. Gall-stone colic, resistant ulceration of the leg, and acute pyrexia of unknown origin may be presenting symptoms. The latter often proves to be associated with a haemolytic crisis. The majority of cases are familial (Race, 1942). The prognosis following splenectomy is excellent. It is essential at operation to remove any accessory spleens and to remember that gall-stones are a common complication.

Sickle cell anaemia

Acholuric jaundice

March haemoglobinuria

March haemoglobinuria is a rare condition occurring in healthy young adults following severe exercise (Gilligan and Blumgart, 1941). The cause is obscure. No treatment is needed.

(2) Disorders of leucopoiesis

(a) *Leucocytosis*

(i) *Neutrophil polymorphonuclear cells.*—Apart from hyperplasia of haemopoietic tissue an increase in circulating neutrophils occurs in the following conditions. *Occurrence*

(1) in response to pyogenic, especially coccal, bacterial infection;

(2) intoxications such as uraemia, illuminating-gas poisoning, lead poisoning, the acute stages of gout and sometimes in poisoning from turpentine, acetanilide, potassium chlorate and arsphenamines;

(3) following acute haemorrhage.

(ii) *Eosinophil polymorphonuclear cells.*—An increase in the circulating eosinophils occurs.

(1) in worm infestation, particularly trichiniasis;

(2) in periarteritis nodosa;

(3) in allergic conditions;

(4) in skin diseases;

(5) during convalescence from an infection;

(6) in tropical eosinophilia.

Leucocytosis associated with a localized infection is often associated with localized glandular enlargement.

(iii) *Lymphocytes.*—A great increase in circulating lymphocytes is characteristic of whooping-cough; a less marked increase is found in German measles, mumps, undulant fever, and by some observers is thought to be characteristic of tuberculosis when the resistance is good. A relative increase in lymphocytes occurs in those infections associated with a leucopenia particularly in the enteric group. An increase of normal and abnormal lymphocytes which are often confused with monocytes is also found in infectious mononucleosis, which presents great difficulties in diagnosis since its manifestations are extremely varied. The characteristic case shows pyrexia, a sore throat, and generalized glandular enlargement sometimes associated with splenomegaly. There may be a leucocytosis or a leucopenia, the predominant cell is a rather young lymphocyte often confused with a monocyte. The serum contains an abnormal agglutinin which agglutinates sheep cells. It is absorbed by ox cells and not by guinea-pig's kidney. A somewhat similar agglutinin is present in low titre in other conditions and it is only of diagnostic significance if found in a titre of 1 : 64 or higher. The test is called after the men who first described it as the Paul-Bunnell test. A closely similar clinical picture is seen in patients giving a negative Paul-Bunnell test. The exact relationship of the two conditions and the significance of the test is still debated. *Infectious mononucleosis* *Characteristics* *Paul-Bunnell test*

A differential diagnosis must be made from monocytic or lymphocytic leukaemia, Hodgkin's disease and agranulocytosis. The latter may sometimes be present with glandular enlargement and the diagnosis is difficult. In the case of the leukaemias or Hodgkin's disease there is usually an associated anaemia which is not present in infectious mononucleosis. *Differential diagnosis*

(iv) *Monocytes.*—The monocytes of the blood are rarely increased except in association with hyperplasias of the sinus reticulum and with tetrachlorethane poisoning.

Acute haemolytic anaemia

There is a large group of unexplained haemolytic anaemias (Dameshek and Schwartz, 1940). In the acute form there is usually sudden profound anaemia of the haemolytic type associated with fever. If very severe, immature white cells as well as red cells may appear in the peripheral blood, so that the picture simulates that of acute leukaemia. No family history is present and no cause can be found. The prognosis on the whole is good. The effects of splenectomy performed as an emergency measure are often striking (Dameshek and Schwartz, 1940). Transfusion alone in some cases is equally dramatic. In the chronic type, splenomegaly is invariably present, the anaemia is not severe and the sternal marrow picture is one of normoblastic hyperplasia. Splenectomy in such cases is often successful.

Chronic haemolytic anaemia

The diagnosis of symptomatic haemolytic anaemia (Davis, 1944) associated with other conditions such as lymphatic leukaemia or Hodgkin's disease should be accepted with caution unless pigment excretion is analysed.

(4) Unclassified anaemias

"Splenic anaemia"

The term splenic anaemia or Banti's disease is used to cover a group of ill-defined conditions, of which the commonest is hepato-lienal fibrosis, associated with hypertension in the portal vein. This is due to some obstruction which may be intra-hepatic or extra-hepatic (Whipple, 1941). It is characterized by splenomegaly, a mild degree of anaemia of a hypochromic type and leucopenia. In the later stages there may also be enlargement of the liver, and oesophageal varices; the latter may give rise to severe haemorrhage. The possibility of splenic anaemia as the cause of unexplained haematemesis must always be considered. The anaemia often responds well to iron. Eliason and Stevens (1943) advocate splenectomy even in the presence of cirrhosis of the liver, but the majority of observers favour more conservative treatment. Injection of the oesophageal varices has recently proved to be successful in some cases in preventing further haemorrhage.

Portal hypertension

Treatment

7. DISORDERS OF THE BLOOD AND BLOOD-FORMING ORGANS (*continued*)

(1) The white cells

Factors controlling leucopoiesis

Little is known of the normal function of the white cells and of the factors controlling their production. Evidence is, however, accumulating which suggests that certain chemical factors are required for white cell production, as they are for red cell production. Recent experimental observations have shown that agranulocytosis produced in monkeys by a modified Goldberger diet (Wilson and his colleagues, 1942), and in rats by feeding sulphonamides (Nielson and Elvehjem, 1942; Daft and Sebrell, 1942; Axelrod and his colleagues, 1943) is relieved by folic acid concentrates and crystalline folic acid. The anaemia and leucopenia which develop in rats fed on a diet deficient in pantothenic acid is relieved by pantothenic acid (Carter and his colleagues, 1945). It is suggested that the normal folic acid requirements are supplied by intestinal bacterial synthesis, and that sulphaguanidine acts by inhibiting this synthesis (Axelrod and his colleagues, 1943).

Folic acid

(d) *The leukaemias*

(i) *Definition.*—Leukaemia may be defined as a fatal systemic disease of unknown aetiology characterized by disorderly hyperplasia of the leucopoietic elements of the reticulo-endothelial system. This hyperplasia is manifested by the presence at some time of abnormal white cells in the peripheral blood, but not necessarily by a leucocytosis. *Definition*

(ii) *Classification.*—Any classification of the leukaemias in the present stage of knowledge is inevitably unsatisfactory since the aetiology is obscure and the origin of the cells of the blood and the character of their precursors in the tissues are disputed. Recent work makes it clear that hyperplasias of the reticulo-endothelial system may take many forms of which leukaemia is only one (Forkner, 1938; Robb-Smith, 1938). *Classification*

Three main types of leukaemia are commonly recognized: (1) Myelogenous; (2) Lymphocytic; (3) Monocytic. The myelogenous type may be further divided into neutrophil, eosinophil and basophil. The two latter are extremely rare.

A further type, namely plasma cell leukaemia, is more commonly considered to be a form of myeloma, though an attempt has been made to differentiate the two conditions. It may be recognized by the occurrence of plasma cells in the circulating blood, but more commonly by finding masses of plasma cells in the marrow on sternal puncture, in conjunction with other physical signs discussed elsewhere. *Plasma cell leukaemia*

(iii) *Clinical picture.*—Leukaemia may occur in an acute or chronic form. It may be associated with a raised white cell count or with a normal or reduced count. In the latter case it is spoken of as sub-leukaemic or aleukaemic. The degree of enlargement of the liver, spleen and glands depends upon the type of cell involved in the hyperplastic process. Enlargement of the spleen and liver is most marked in myelogenous leukaemia; enlargement of the glands in lymphatic leukaemia. Enlargement of the spleen alone is commonly found in monocytic leukaemia. The differential cell count shows a predominance of the cell type involved. In the case of chronic lymphatic leukaemia, and in some cases of chronic monocytic leukaemia, the predominant cell is mature. In all cases of chronic myelogenous leukaemia, and in some cases of chronic monocytic leukaemia, immature cells are found, sometimes in large numbers. In acute leukaemia of all types immature cells are present in the peripheral blood though they may be few in number, since acute leukaemias are often aleukaemic. *Acute and chronic* *Blood picture*

There is almost invariably a severe anaemia with a tendency to haemorrhage particularly from the nose and gums. Platelets are greatly reduced.

Pyrexia associated with angina and ulceration of the gums are the commonest presenting symptoms in acute monocytic leukaemia. A history of a recent visit to the dentist is particularly characteristic of this type. Nodules in the skin are found and may also be the presenting symptoms. *Other symptomatology*

In children bone and joint pains are often presenting symptoms especially in acute lymphocytic leukaemia. A diagnosis of acute rheumatism or osteomyelitis is often made. Scurvy has also, though more rarely, been confused with acute leukaemia. Skiagrams may show elevation of the periosteum due to leukaemic infiltration (Poynton and Lightwood, 1932; Snelling, Brown and Erb, 1934). This may be associated with proliferation of new bone at *Bone change*

(b) *Leucopenia*

Occurrence

A moderate reduction in the number of circulating white cells usually affects the neutrophil polymorphs rather than the other cell types. This may occur in profound infections and, in such cases, is of bad prognosis. Leucopenia is characteristic of typhoid fever, and is less often seen in paratyphoid A and paratyphoid B infections. In Addisonian pernicious anaemia and in sprue it is almost invariable. It occurs in aplastic conditions of the bone marrow and to a moderate extent in splenic anaemia. Recently a group of cases has been described as splenic neutropaenia, in which there is long-standing agranulocytosis and splenomegaly without anaemia (Rogers and his colleagues, 1945; Langston, White and Ashley, 1945). The lack of anaemia and of fibrosis in the spleen at operation differentiates these cases from splenic anaemia. The response to splenectomy so far has been good. A great reduction in white cells usually associated with a sudden fall in red cells and platelets may follow exposure to certain toxic substances particularly benzol, thorium, arseniuretted hydrogen and arsenic. Leucopenia characteristically affects the lymphocytes rather than the polymorphs in excessive exposure to x-rays or radium.

Splenic neutropenia

Toxic substances

(c) *Agranulocytosis*

An almost complete absence of neutrophils and a great reduction of other white cells in the peripheral blood, without changes in the red cell picture, occur in susceptible individuals following the administration of certain drugs. A dose as small as 0·6 gramme of amidopyrine may precipitate profound changes in leucopoiesis resulting in the arrest of white cell development, agranulocytosis, fulminating angina and death.

Dangerous drugs

The commonly effective drugs are those containing a benzene ring, such as the sulphonamides (Park, 1944) or amidopyrine (Plum, 1937); more recently a few cases have been described following thiourea or thiouracil (Astwood, 1943).

The finding of an unexplained leucopenia should always arouse suspicion that one of these drugs is involved. The patient's negative answer cannot be accepted as both amidopyrine and sulphonamides are liable to be taken in an unrecognized form. Sulphonamides, for instance, are sometimes given as a throat spray, and amidopyrine is included in certain "pick-me-ups". The occurrence of leucopenia and generalized glandular enlargement may be associated with sulphonamide poisoning as well as with glandular fever or leukaemia. Examination of a sternal marrow puncture often will be of value in the differential diagnosis. In leukaemia there is proliferation of a predominant cell type. In glandular fever, apart from a possible excess of lymphocytic cells, there is no abnormality, whereas in agranulocytosis the marrow, though showing excessive cellularity and some abnormal cells, shows no predominant cell.

Sulphonamides

Amidopyrine

Differential diagnosis

Burns

Occasionally agranulocytosis is seen following severe burns.

Treatment

The evidence already discussed, showing that elements of the vitamin B complex may relieve experimental agranulocytosis due to sulphonamides in animals, suggests that a trial should be made of heavy vitamin B dosage and of folic acid, if available, in such cases in human beings. Pentose nucleotide has proved disappointing. Transfusions with fresh blood are indicated.

there is often a high malar colour. Anaemia may be severe. The differential cell count shows immature myeloid cells of all types. Extremely young red cells are characteristic. The picture is that of classical leuco-erythroblastic anaemia. On sternal puncture no characteristic cavity is appreciable. The marrow withdrawn is usually highly cellular often showing many megakaryocytes and both young red and white cells, whereas in the other leukaemic conditions one cell of the white cell series predominates.



Fig. 65.—Skiagram of radius and ulna in acute lymphocytic leukaemia. Note rarefaction of lower ends of bones.

Diagnosis

The diagnosis of myelosclerosis can be confirmed in the majority of cases by radiographic examination of the skeleton. Bony involvement is common in all types of leukaemia; there is rarefaction and erosion due to invasion of bone by leukaemic tissue (Fig. 65). In myelosclerosis on the other hand there is often widespread sclerosis (Fig. 66).



Fig. 66.—Skiagram of tibia and fibula in case of myelosclerosis. Note irregular, increased density of the upper end, and irregularity of the inner edge of the cortex; also well-marked sclerosis of vessels.

Transfusion

(v) *Treatment*.—No treatment is of any avail in acute leukaemia. Transfusion may prolong life for a few days or weeks but without great amelioration of symptoms. In chronic leukaemia, x-ray treatment enables the patient to lead a comparatively active life until a few weeks before death which is usually precipitated by an acute infection. In myelosclerosis the results of the transfusion are often dramatic.

X-ray

(e) *Lymphadenopathies without blood or marrow changes*

Lymphadenopathies

In certain lymphadenopathies no changes are found in the blood picture or the marrow. For an analysis of these, reference should

right angles to the shaft, suggesting sarcoma (Fig. 64). Extreme generalized osteoporosis and irregular cortical absorption leading to spontaneous fracture may occur (Baty and Vogt, 1935). Bones of the skull may show diffuse granular mottling and the sutures separate as a result of intracranial pressure. Retinal changes are found most often in myeloid leukaemia.

The diagnosis, which it is often impossible to make from the blood picture alone in the acute form, particularly in monocytic leukaemia, can always be confirmed by sternal puncture which, in the case of leukaemia, will reveal an



FIG. 64.—Skiagram of lower end of femur and upper end of tibia and fibula with normal control, in case of lymphocytic leukaemia. Note irregular, increased density of femur.

extremely cellular marrow with one atypical or extremely young cell type predominating.

Lympho-sarcoma

(iv) *Differential diagnosis.*—The differential diagnosis of leukaemia from other conditions can be made usually with more certainty by examination of the sternal marrow than from gland biopsy or the blood picture alone, except in the chronic types of leukaemia. Every case of glandular enlargement, of severe stomatitis and angina, and of acute bone pain should have the blood picture examined and, if anaemia is present, a marrow biopsy should be performed in order to rule out the possibility of a leukaemic condition. The relationship of lymphatic leukaemia and lymphosarcoma is uncertain. In rare cases a leukaemic blood picture may be associated with enlargement of one group of glands only, usually the mediastinal, which infiltrate surrounding tissues. Lymphosarcoma is more usually associated with a normal blood picture. The treatment and prognosis in both conditions are similar.

Myelo-sclerosis

It is important to distinguish between chronic myeloid leukaemia and myelosclerosis, since the treatment of the two is different. In myelosclerosis there is great splenic enlargement, with slight glandular involvement;

and the dilution is 1 in 200. Therefore the number of cells in 1 cubic millimetre when N cells are counted is

$$N \times 10 \times 200 \times 5$$

(*c*) *White blood cell counts*

Suck blood up to the 0·5 mark on the white cell counting pipette and white cell diluting fluid up to the 11 mark, giving a dilution of 1 in 20. Mix well by shaking for three minutes. Fill the Neubauer counting chamber. All the white cells in the 4 large corner squares are counted. The depth of the chamber is $\frac{1}{10}$ millimetre. The area counted is 4 square millimetres and the dilution is 1 in 20. Therefore the number of cells in 1 cubic millimetre when N cells are counted is

$$\frac{N \times 20 \times 10}{4}$$

(2) Mean corpuscular volume

5–10 cubic centimetres of blood obtained by venepuncture without constriction are added to heparin or a mixture of ammonium and potassium oxalates (0·1 millilitre of 2 per cent solution containing four parts potassium oxalate and six parts ammonium oxalate for every millilitre of blood, dried in a test tube). After mixing, blood is withdrawn by means of a Pasteur pipette, and a Wintrobe haemotocrit tube filled to the 10-centimetre mark. This is then centrifuged for half an hour at 3,000 revolutions per minute and the volume of packed cells then read. Mean corpuscular volume =

$$\frac{\textit{Volume of packed red cells in cubic millimetres per 1,000 cubic millimetres}}{\textit{Number of red cells per cubic millimetre}}$$

The normal range 78-94 cμ.

(3) Haemoglobin estimation

As already discussed (*see* page 163), estimation of haemoglobin though done so constantly is still far from exact owing to difficulty in determining either the oxygen content or iron content of human haemoglobin. Though it is desirable, it is not at present possible to express haemoglobin in grammes per cent. The best that can be done is to express it in terms of a colour standard prepared by the National Physical Laboratory according to B.S.I. specification No. 1079, 1942 (Macfarlane and his colleagues, 1944; Medical Research Council *Special Report Series* No. 252, 1945). Such a standard is now available for the Haldane carboxyhaemoglobin method and, it is hoped, will be available shortly for the Sahli (acid haematin) method.

All apparatus should be certified by the National Physical Laboratory. Blood may be obtained from a finger or ear prick or by venepuncture, being in the latter case added to a solid anti-coagulant such as heparin or a mixture of ammonium and potassium oxalates. For approximately 1 millilitre of blood to be taken 0·1 millilitre of 2 per cent solution, containing four parts potassium oxalate and six parts ammonium oxalate, should be dried in the bottom of a test tube.

(*a*) *The Haldane method*

The principle of this method is that the oxyhaemoglobin is converted into carboxyhaemoglobin and matched against an artificial glass standard. On the National Physical Laboratory scale 100 per cent is the equivalent of

be made to the detailed review by Robb-Smith (1938). The diagnosis in the majority of such cases is a histological one, and can be made with certainty only by experienced workers.

8. METHODS OF EXAMINATION

(1) Total cell counts

Blood may be taken from an ear or a finger prick or by venepuncture. Constriction should not be applied. In the case of the ear it should be well rubbed with ether and then pricked. Remove the first drop of blood with cotton-wool. Suck blood up to the 0·5 mark on the cell diluting pipette, and then suck diluting fluid (1 cubic centimetre of 1 per cent gentian violet in 100 cubic centimetres of normal saline) up to the 101 mark, giving a dilution of 1 in 200. Mix well by shaking for three minutes.

Blow out the first few drops of fluid. Fill a Buerker or other counting chamber so that no fluid runs over the ditch but the chamber itself is completely filled. Examine under a $\frac{1}{6}$-inch objective.

(a) Enumeration of red cells in a Buerker counting chamber

The ruled area on a Buerker counting chamber has an area of 9 square millimetres. It is marked by treble vertical and transverse lines into 9 squares each 1 square millimetre in area. Each small square is further divided by three vertical and three transverse sets of two lines. The width between these two lines is $\frac{1}{20}$ millimetre. The depth between the coverslip and the floor of the cell is $\frac{1}{10}$ millimetre.

(b) To count red cells

Take one of the single $\frac{1}{20}$-millimetre columns and count all the red cells throughout the length of the column, that is 3 millimetres. If N red cells are counted in such a column, the number of red cells in 1 cubic millimetre will be

$$\frac{N \times 200 \times 10 \times 20}{3}$$

In practice it is better to count 3 of these columns and take the average of the three. They should not differ by more than 10 cells.

(c) To count white cells

The white cells may be counted in the same sample of blood since they are stained blue by the gentian violet. The white cells seen in the entire ruled area must be counted. If N white cells are seen, the number in 1 cubic millimetre of blood will be

$$\frac{N \times 200 \times 10}{9}$$

(d) Enumeration of cells in a Neubauer counting chamber

The ruled area on a Neubauer counting chamber has an area of 3 square millimetres divided into 9 large squares; the 8 outside squares are subdivided into 16 smaller squares. The central square is divided into 400 small squares, through 144 of which triple lines are drawn, leaving 256 small squares in groups of 16. Count the red cells in 5 groups of 16 small squares or 80 small squares in all.

The depth of the chamber is $\frac{1}{10}$ millimetre. The area counted is $\frac{1}{5}$ millimetre

centrifuged cells respectively. By assuming normal values of 33·9 for H and 1·0970 for G, the haemoglobin can be calculated from the blood and plasma specific gravities; and by further assuming a normal value of 1·0264 for the plasma specific gravity the haemoglobin can be calculated from the blood specific gravity alone.

Copper sulphate solutions.—Stock solution of copper sulphate of specific gravity 1·100 is made by dissolving 159·63 grammes of $CuSO_4.5H_2O$ in distilled water to a final volume of 1,000 millilitres. The specific gravity of this solution after filtration is determined by comparing the weight of 100 millilitres with that of 100 millilitres of water.

Standard copper sulphate solutions with specific gravities graded at 0·001 intervals from 1·015 to 1·074 are made by diluting the appropriate volume of stock solution in a 100-millilitre flask. The number of millilitres of stock solution needed to make 100 millilitres of any standard solution is 1 less than the number indicated in the second and third decimal places of the desired specific gravity. For example, to prepare a solution with gravity 1·049 dilute $49 - 1 = 48$ millilitres of stock solution to 100 millilitres. The standard solutions are stored in 6-ounce screw-topped flat bottles.

(d) Specific gravity determinations

Small drops of blood or plasma from a capillary pipette are dropped into the appropriate solutions. The behaviour of the drop during the first 10 seconds is observed. If it remains stationary in a particular bottle it is of that specific gravity; if it rises and falls in adjacent bottles its specific gravity is easily estimated to the nearest 0·0002 by noting the relative speed of rise and fall.

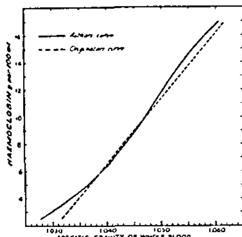


Fig. 67.—Relationship between the haemoglobin content and specific gravity of whole blood. (Unpublished curve supplied by M. Hynes, calculated from his own data.)

To pick out the anaemic members of a group it is only necessary to put one drop of blood from each person into one copper sulphate solution corresponding to the haemoglobin value chosen as the limit. If the drop rises, the individual is counted as anaemic. The relationship between the haemoglobin content and specific gravity of whole blood is shown in Fig. 67.

(4) Estimation of plasma bilirubin

(*a*) *Method of King, Haslewood and Delory* (1937)

The principle of the method is that the red colour produced by bilirubin in the presence of diazotized sulphanilic acid is compared colorimetrically with an artificial standard containing methyl red.

(*b*) *Diazo reagents*

(i) *Solution A.*—Dissolve 1 gramme of sulphanilic acid in 250 cubic centimetres of N_1 hydrochloric acid and dilute to 1 litre with water.

approximately 14·7 grammes of haemoglobin. In a special pipette 0·02 millilitre of blood is taken and is washed out into a graduated diluting tube marked in percentages into which has been put 0·4 per cent ammonia solution (4 millilitres liq. ammon. fort. sp. gr. 0·880 in a litre of distilled water) up to the 20 mark. This is then saturated with coal gas by means of a capillary pipette attached either to the main gas supply or to a cylinder of carbon monoxide gas. Diluting fluid is then added drop by drop with a fine pipette until the colour matches that in the standard tube. In matching, daylight from a north sky should be used, the tubes being viewed either against the sky or against a white or neutral background. The graduated tube should be held first on one side of the standard and then on the other. When the end point has been reached the level of the meniscus should not be read until the tube has stood for three minutes.

(b) The Sahli method

The principle of this method is that the blood when drawn is converted into acid haematin and matched against a brown glass standard. To decinormal hydrochloric acid placed in the diluting tube up to the 10 mark 0·02 millilitre of blood is added by washing backwards and forwards. Distilled water is then added drop by drop until the colour matches the standard. Complete conversion into acid haematin takes place slowly, which is the disadvantage of this method. Results should therefore all be read at a standard time after mixing the blood and hydrochloric acid. In practice this is often done at the end of ten minutes.

(c) The copper sulphate method

To determine whether a large number of individuals have a haemoglobin level within the normal range the copper sulphate method is valuable. This method is probably not satisfactory for pathological bloods, but if it is desired, for instance, to check that large numbers of blood donors have a normal haemoglobin before bleeding, the method is admirable (Philips and his colleagues, 1945; Hynes and Lehman, 1946).

This method is based on the fact that plasma or whole blood dropped into a solution of copper sulphate of known specific gravity is encased in a sack of copper proteinate, and the specific gravity of this discrete drop is not changed for about 15 seconds. The rise or fall of the drop during this interval shows whether it is lighter or heavier than the solution. Thus, by dropping blood or plasma into standard copper sulphate solutions with specific gravities graded at 0·001 intervals, the specific gravity can be determined to ± 0·0002. The solution does not significantly change its specific gravity until one-fortieth of its volume of blood has been added, so that 100 millilitres of solution suffices for nearly 100 observations. The specific gravity of plasma is directly related to the plasma protein content, and this remains the most useful application of the method. It is also known that the haemoglobin can be calculated from the equation

$$\text{Haemoglobin grammes per 100 millilitres} = H \times \frac{G_b - G_p}{G_c - G_p}$$

where H is the grammes of haemoglobin in 100 millilitres of centrifuged cells, and G_b, G_p, and G_c are the specific gravities of the whole blood, plasma and

Wintrobe's method

The tube used for haematocrit determinations is employed. The tube is filled to the 10 mark with blood mixed with heparin or potassium and ammonium oxalates and is allowed to stand for one hour, when the level of the sedimented cells is read off. The volume of packed cells is then determined by centrifuging the tube for half an hour at 3,000 revolutions per minute and the correct sedimentation read off the chart. (*See* Fig. 68.)

(6) Staining of blood and marrow smears

(a) Jenner-Giemsa's stain for marrow films or films showing abnormal white cells

(i) Cover the slide with Jenners stain for 3 minutes.

(ii) Add an equal amount of distilled water to the stain on the slide by means of a Wright's pipette and allow the diluted stain to act for 1 minute.

(iii) Drain the slide but do not wash.

(iv) Place the slide face downwards in a dilute solution of Giemsa's stain —1 drop per cubic centimetre of distilled water—for 8 to 12 minutes. This is done most conveniently in the following way: break off two lengths of capillary tubing about 2 inches long and place them in the bottom of a small petrie dish; make up 10 cubic centimetres of dilute Giemsa's solution and pour it into the petrie dish; then place the slide face downwards in the stain, either end resting on the two pieces of capillary tubing.

(v) Stain for 8 to 12 minutes.

(vi) Wash thoroughly in distilled water.

(vii) Dry and mount.

This method is valuable for staining nuclear detail. In good preparations, the nucleoli are reddish in the thinner parts, and bluish in the thicker ones. The character of the nuclear membrane is clearly seen and nucleoli, if present, appear as paler gaps in the nucleus. Neutrophil granules are violet-red, but differ somewhat according to the age of the cell. The eosinophil granules are red or dark red. Basophil granules are dark purple. In some of the lymphocytes brilliant red azure granules can be seen; in many monocytes similar but much smaller structures of the same colour are present. Red corpuscles stain almost copper-red. Slight degrees of polychromasia are shown by bluish stain.

According to American workers lymphoblasts show the following characteristics. The nuclear chromatin is fine. There are two to three nucleoli, and there is a paler zone in the cytoplasm around the nucleus. Myeloblasts show 4 to 6 nucleoli and there is no paler zone in the cytoplasm around the nucleus. Differentiation, however, between these two types is not always possible. Myeloblasts may occasionally show pseudopodia and Auer's bodies, whereas lymphoblasts do not.

(7) Sternal puncture

Sternal marrow puncture

A variety of special needles has been designed. The "Salah" needle is simple and efficient. If necessary a sawn-off lumbar puncture needle or a transfusion administering needle may be used.

If possible the patient is given $\frac{1}{8}$ or $\frac{1}{4}$ grain of morphine half an hour before the puncture is performed. He lies flat in bed, the head being supported with one pillow. The skin over the sternum is cleansed and then a point in the

(ii) *Solution B.*—Dissolve 0·5 gramme of sodium nitrate in 100 cubic centimetres of water.

The reagent is freshly prepared, as required, by mixing 0·3 cubic centimetre of solution B with 10 cubic centimetres of solution A.

(*c*) *Standard*

(i) *Stock methyl red solution.*—Dissolve 0·29 gramme of pure methyl red in glacial acetic acid and dilute with acid to 100 cubic centimetres.

(ii) *Standard methyl red solution.*—One cubic centimetre of the stock solution, 5 cubic centimetres of glacial acetic acid and 14·4 grammes of crystallized sodium acetate are made up to 1 litre with water. This solution at *p*H 4·63 contains 2·9 milligrams of methyl red per litre and matches the colour obtained when 0·1 milligram of bilirubin is treated with diazo reagent in a final volume of 25 cubic centimetres.

(*d*) *Method*

Quantitative reaction.—One cubic centimetre of plasma or serum is treated in a centrifuge tube with 0·5 cubic centimetre of diazo reagent, 0·5 cubic centimetre of saturated ammonium sulphate and finally 3 cubic centimetres of absolute alcohol. The mixture is stoppered, thoroughly shaken, and filtered after a few minutes. The colour of the filtrate is matched against the standard in the colorimeter, using a green light-filter. The reading of the standard divided by the reading of the unknown and then multiplied by 1·6 gives the number of milligrams of bilirubin per 100 cubic centimetres of plasma or serum.

Direct reaction.—If the diazo reagent is carefully "layered" above the plasma and the tube allowed to stand for a few moments, a positive "direct" reaction is shown by a red colour at the junction of the liquids.

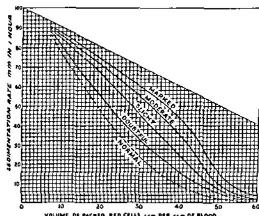


FIG. 68.—Chart showing correction of sedimentation rate for anaemia ascertained after determining the corpuscular volume. To determine the correction find the junction of the lines of the sedimentation rate as estimated and the ascertained corpuscular volume. (This point falls within one of the five zones marked and indicates the approximate degree of increase in the rate.)

To arrive at a definite compensated figure follow the curve to the point where it cuts the 45 cubic centimetre thick vertical line (average corpuscular volume).

Example: Observed rate = 68 millimetres; observed corpuscular volume = 20 cubic centimetres; point of junction lies in area of "moderate" increase; compensated rate = 22 millimetres. (Whitby and Hynes, 1938b.)

(5) Sedimentation rate

Two methods are in common use, that of Wintrobe and that of Westergren. The former is more readily corrected for the degree of anaemia, which is important, and is therefore described here. In both it is absolutely essential that the tubes should be kept in a vertical position during the test. The stand should therefore be fitted with a spirit level.

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midline over the manubrium or first part of the sternum is infiltrated, together with the subcutaneous tissue and periosteum, with local anaesthetic, using about 2 cubic centimetres. The needle to be used for puncture is then taken in the right hand and inserted vertically with a slight rotatory movement through the infiltrated area into the marrow cavity. It should be remembered that in young adults considerable force may be required; the risk of going through into the mediastinum is slight since the passage of the needle through the bone into the marrow cavity is usually readily appreciated, even by an onlooker. There is a sudden "give" and often an actual "scrunch" is heard as the cavity is reached. If a stilette is present it is now withdrawn and a syringe attached to the needle; a bead of marrow only should be withdrawn. If more is taken it is liable to become diluted with blood. The syringe is then disconnected and smears made in the usual way. After removal of the needle the puncture hole is sealed with collodion. Smears may also be made from the marrow retained in the needle. The smears should be stained with Leishman's or Jenner-Giemsa's stain.

Some authorities advise making total counts of mature red and nucleated red cells and white cells in a counting chamber after mixture with diluting fluid. This procedure is unsatisfactory as the white cells tend to clump and the degree of dilution with blood is not capable of measurement. Experience will soon teach the observer whether or not the sample withdrawn is unduly cellular.

DISTRIBUTION OF CELLS IN NORMAL MARROW

LEUCO-ERYTHROBLAST RATIO, 8 : 1–2 : 1

Haemocytoblast	0–1
Primary erythroblast	2–7
Normoblasts	7–19
Megaloblast (not usually seen)	0–1
Myeloblast	0–2·5
Premyelocytes	0·5–5
Neutrophil myelocytes	2–8
Neutrophil promyelocytes	2·5–12
Neutrophil polymorphonuclears	20–50
Eosinophil myelocytes	0–4
Eosinophil promyelocytes	0–2·5
Eosinophil polymorphonuclears	0–4
Basophil polymorphonuclears	0–1
Lymphocytes	5–20
Monocytes	0–5
Plasma cell	0–1
Megakaryocytes	0–1
Undifferentiated cells	0–2

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BLOOD-PRESSURE: HIGH AND LOW

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1. HIGH BLOOD-PRESSURE

(*synonym*—Hypertension)

(1) Definition

61.] There is hypertension when the blood-pressure is 170 millimetres of mercury systolic and 90 millimetres of mercury diastolic. Lower pressures may be pathological. A distinction is made between transient and persistent hypertension. Transient hypertension is often due to emotional stress, to emotional or physical fatigue, or it may be spontaneous. It may presage persistent hypertension, particularly if the diastolic pressure is 100 millimetres of mercury or over.

Transient hypertension

(2) Measurement of blood-pressure

The blood-pressure should be taken with the patient reclining on a bed or couch, in the first place by auscultation of the brachial artery at the bend of the elbow, and in the second place by palpation of the radial artery. The tactile pressure must agree within 10 millimetres with the auditory reading. It may be the same as the auditory reading, but if the tactile pressure is higher than is the auditory pressure (unless one of the readings is faulty), it shows the presence of a silent gap. This is confirmed by repeating the auditory reading with the precaution that the pressure in the manometer is raised 20

The silent gap

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an open question, but there is no doubt that emotional and physical fatigue and strain, especially if long continued, aggravate hypertension. To some extent obesity, diabetes mellitus, gout and osteoarthritis belong to the same constitutional make-up as essential hypertension.

Constitutional type

(4) Pathology of hypertension

The relation of arteriosclerosis to hypertension is best understood by an approach to its consideration from three angles. In the first place Aschoff's view is generally accepted that arteriosclerosis and arteriolosclerosis can be considered together, because the two conditions so often are associated, and because their pathological processes are so similar. In the second place it has been shown by post-mortem studies that arteriolosclerosis (*synonym* diffuse hyperplastic sclerosis) is nearly always present in the bodies of persons the subject of established hypertension during life (Evans, 1921). In the third place Moschcowitz has assembled evidence in favour of the view that normal intravascular pressure and its increased gradient hypertension acting over a period of time is the important cause of arteriosclerosis. He submits that hypertension precedes arteriosclerosis, and not conversely. Goldblatt's work suggests that one of the causes of persistent hypertension is renal ischaemia (Goldblatt, 1940). This is confirmed by clinical experience in the case of unilateral kidney disease, because in the case of some children and young adults hypertension has been relieved by removing the diseased kidney.

The relation of arteriosclerosis to arteriolosclerosis

The relation of arteriolosclerosis to hypertension

The relation of arteriosclerosis to hypertension

Renal ischaemia a cause of hypertension

(5) Diagnosis of essential hypertension

The diagnostic sign of hypertension is a diastolic pressure of 90 millimetres of mercury or over. In certain conditions, such as shock and severe haemorrhage, the blood-pressure may fall to a normal or subnormal level, and yet hypertension may be recognized, or at least strongly suspected, by the thickening of the radial artery (due to hypertrophy of its middle coat), accentuation of the aortic second sound and, perhaps, by evidence of left ventricular hypertrophy and retinal arteriosclerosis. In a patient who has had a severe haematemesis these signs of persistent hypertension may be of diagnostic significance, as being evidence that the haemorrhage is due to arteriosclerotic disease (Evans, 1944) and not to peptic ulceration. The diagnosis of essential hypertension is made only after excluding renal disease and the causes of symptomatic hypertension. It is advisable to do intravenous pyelography in the case of children and young adults with hypertension in order to exclude unilateral kidney disease. On account of the difficulty of excluding kidney disease, and because the development of malignant hypertension from the benign form is on occasion so insidious, it is a wise precaution to do a blood urea estimation on all patients with hypertension. If the urine shows any abnormality, renal function tests should also be done.

(*a*) *Benign hypertension*

A distinction is made between benign and malignant forms of essential hypertension according to whether or not the kidneys are involved in the disease. Arteriosclerotic disease, of which hypertension is a symptom, though widely distributed through the body, tends to involve some areas more than others. As a result of this regionalization of the disease, it may declare itself in one subject in the form of a cerebral vascular disturbance, angiospastic

Cerebral type

millimetres above the tactile reading. The silent gap is not uncommon in hypertension and aortic stenosis. If the tactile reading is more than 10 millimetres below the auditory reading of the systolic pressure the blood-pressure is taken again. It will be found to be lower, and the reading is recorded when tactile and auditory levels are within 10 millimetres. This fall of pressure with repeated compression of the brachial artery is due to relaxation of the muscle of the middle coat of the artery (Oliver, 1916).

(3) Classification of hypertension

(*a*) *Renal hypertension*

Urinary disease

Hypertension is one of the cardinal signs of acute and chronic nephritis, and of polycystic disease of the kidneys. Even the severest forms of nephritis, including renal dysbiotrophy (Price, 1941), may, however, run their whole course to a fatal termination without hypertension; in fact, there may be hypotension in their later stages. Other known urinary causes of persistent hypertension are chronic pyelonephritis, hydronephrosis and obstruction to the flow of urine in any part of the urinary tract. A number of rare causes of persistent hypertension includes renal tumours, narrowing of the lumen of the renal artery, generally due to arteriosclerosis, and periarteritis nodosa when the renal arteries are seriously implicated (Fishberg, 1944).

(*b*) *Symptomatic hypertension*

Endocrine diseases

Suprarenal tumours

Pituitary disease

Graves's disease

The presence of hypertension should bring to mind the possibility of certain endocrine diseases. Attacks of paroxysmal hypertension, which may lead to persistent hypertension, are characteristic of adrenal blastomas. These tumours are generally of the chromaffin-celled variety, or phaeochromocytomas. The results after removal of the tumour have been brilliant (Moschcowitz, 1942). Persistent hypertension is one of the diagnostic signs of Cushing's syndrome. Its association with Graves's disease is well known. When, as commonly happens, persistent hypertension develops in a person with Graves's disease of long standing, the association is probably due to a constitutional predisposition to both Graves's disease and persistent hypertension rather than to a direct sequence of cause and effect. With regard to climacteric hypertension, it is quite probable that the hypertension results from a disturbance of the interrelation of the ovaries with other endocrine glands, and that women who develop hypertension in relation to either an artificial or natural menopause have a hereditary tendency to it (Fishberg, 1944).

Climacteric hypertension

Toxic causes

Coarctation of aorta

As to other causes of persistent hypertension, pregnancy toxaemia, and lead and mercury poisoning, are the only agreed toxic causes. There is no convincing evidence that syphilis, malaria or focal sepsis are aetiological factors. Coarctation of the aorta is a rare cause of hypertension.

(*c*) *Essential hypertension*

Aetiology

Apart from urinary disease, the great majority of cases of persistent hypertension come within the category of essential hypertension. The only established factor in its aetiology is an inherited constitutional predisposition. This applies not only to an inherited tendency to develop the disease exhibited by certain families, but also to an inherited tendency in the case of some families to develop the disease at a certain age or even in a certain region, such as the brain or heart. The effect of environment in initiating hypertension is still

(2) Anaesthesia

The choice of a general anaesthetic is made in order best to safeguard the heart and to avoid respiratory complications following anaesthesia, because patients with hypertension are potential candidates for heart failure. A severe fall of blood-pressure should be avoided, and therefore a spinal anaesthetic should not be above the level of D.10 (Evans, F. T., 1942).

(3) Operation

Hypertension introduces no particular complication of actual surgical technique, except that extra care needs to be taken in tying all bleeding points, and haemorrhage may increase the difficulty of sinus and nasal operations. This difficulty may also be experienced in enucleation of the tonsils.

(4) Post-operative complications

One of the factors predisposing to post-operative thrombosis is an appreciable fall of blood-pressure in an hypertensive or arteriosclerotic subject. Special care, *therefore, should be taken to maintain the functional efficiency* of the cardiovascular system after operation. Local injury may be a cause of either arterial or venous thrombosis. Thus, pressure on the bend of the knee when the patient is in the lithotomy position may be a cause of popliteal artery thrombosis. *With the object of preventing venous thrombosis* exercises for the muscles of the feet, legs and trunk, and breathing exercises, are helpful.

3. LOW BLOOD-PRESSURE

(*synonym*—Hypotension)

(1) Definition

Whereas in respect of high blood-pressure the diastolic pressure has the greater significance, the term low blood-pressure is applied to a low systolic pressure. The lower limit of normal systolic pressure is 110 millimetres of mercury. There are occasional exceptions even to this figure. The blood-pressure is certainly pathological if it is 100 millimetres of mercury or under, and figures well above this level may, of course, be pathological for a particular individual. The diastolic pressure is proportionately less affected than is the systolic.

(2) Aetiology

A low blood-pressure may run in families, and provided it is above 100 millimetres of mercury can be physiological. Hypotension is one of the cardinal signs of Addison's disease, although it is not always present in this disease. It also occurs in pulmonary tuberculosis and diphtheria. It results from shock, severe haemorrhage and coronary thrombosis; and may occur in convalescence from debilitating disease, in malnutrition and cachexia.

(3) Clinical picture

The patient complains of weakness and of fatigue on physical or mental effort. *He feels giddy on standing up*, or even on sitting up in bed after lying down, there may be faintness. There is tachycardia on slight exertion or on change of posture. The hands and feet are cold.

Other types

symptoms, thrombosis or haemorrhage. In another subject its major manifestations may be in the form of hypertensive heart disease, mesenteric thrombosis, or peripheral vascular disease (Collens and Wilenski, 1939). Although these developments or complications of essential hypertension are serious, and often fatal, they are nevertheless classed together under the term benign hypertension.

(*b*) *Malignant hypertension*

Renal type

This is recognized by evidence of kidney disease, and particularly by the presence of papilloedema and retinal exudates (hypertensive retinopathy). It is characteristic of malignant hypertension that the diastolic pressure is more than 120 millimetres of mercury. The systolic pressure is generally over 220 millimetres of mercury. The patient complains of malaise, loss of energy and fatigability, tends to lose weight and to develop anaemia. When the condition is established the urine is pale, of low fixed specific gravity and contains albumin. Hyaline, granular and epithelial casts are present, and the deposit is also likely to contain excess of red and white blood corpuscles. As renal function fails, in addition to loss of power of concentrating urine, the

Uraemia

blood urea rises and uraemia develops. The urine in benign hypertension may contain a trace or thin cloud of albumin, but it is clear, and it has a good colour and specific gravity because renal function is good. In some 10 per cent of cases benign hypertension develops into malignant hypertension.

Prognosis

The prognosis in malignant hypertension is very serious. In the great majority of cases it is a progressive disease ending fatally in uraemia within one or two years of its diagnosis. In exceptional cases it reaches a quiescent phase, and an invalid life may be prolonged even five or six years. Life may be cut short by a cerebral vascular accident, hypertensive heart failure, coronary thrombosis or intercurrent disease.

2. IMPLICATIONS OF HYPERTENSION IN RESPECT OF SURGERY

(1) Prognosis

Family history, past history, as well as present condition, are taken into account in assessing the expectation of life in a patient who has essential hypertension of the benign type. If cerebral or cardiac complications have developed, the expectation of life is considerably shortened. In favourable cases the disease may be quiescent for periods of three to five or even fifteen years, and occasionally longer. Thus a man may be free of symptoms and feel well with a blood-pressure of 210/100, and the older the patient the more likely is he to survive with a raised blood-pressure. Active phases of the disease

Active and quiescent phases of arteriosclerotic disease

(arteriosclerotic disease) are recognized by haemorrhage from any organ; haemoptysis, haematemesis, melaena, menorrhagia and epistaxis are common. Retinal haemorrhages and microscopical haematuria (occasionally frank haematuria) are most common. *Pain is the cardinal symptom* of the disease. It may be cerebral, cardiac or "rheumatic". It seems that in some cases an active phase of arteriosclerotic disease lasting some months can be recognized, and this may be followed by a quiescent phase lasting one, two or more years. In other cases the disease is steadily progressive, and in malignant hypertension necessarily so in nearly all cases.

BLOOD TRANSFUSION—PRACTICE

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4. IMPLICATIONS OF HYPOTENSION IN RESPECT OF SURGERY

(1) Pre-operative treatment

So far as is possible hypotension should be corrected before any major surgical procedure is undertaken. When it is due to myocardial disease it is a contra-indication to operative treatment.

(2) Anaesthesia

Low blood-pressure is a contra-indication to spinal analgesia.

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aplastic anaemia. Many conditions, however, requiring surgical intervention —for example neoplastic disease, various gynaecological and obstetrical disorders and some chronic infective conditions—are complicated by chronic anaemia, which may be refractory to medical treatment, or must be combated rapidly. Cachexia may also be present with a subnormal plasma-protein level. Anaemia and hypoproteinaemia not only increase the surgical risk but impede wound healing. Such patients should be transfused before operation to raise the haemoglobin and plasma-protein levels to the normal range.

(5) Platelet deficiency

Essential thrombocytopenia is characterized by a reduced platelet count, the restoration of which to a normal level may tide over an acute phase of the disease.

(6) Other clotting elements

Transfusion arrests haemorrhage in haemophilia by supplying some agent whose nature is not known. Damage to the liver is accompanied by reduction in prothrombin or fibrinogen or both, the provision of which by transfusion will reduce the tendency to bleed.

(7) Leucocytes

In infective conditions leucocytes are provided by the transfusion of fresh blood. Their value is unproved.

(8) Immune bodies

Certain non-specific elements, such as complement, are sometimes of value in infections or septicaemia, and may be provided by the transfusion of fresh blood. Specific immune-transfusions, in which the donor has been previously immunized, have been practised with doubtful success.

3. TRANSFUSION FLUIDS AND THEIR USES

The following fluids other than crystalloids are available for transfusion: fresh citrated blood; stored citrated blood; concentrated red cells; serum (fluid or dried); plasma (fluid or dried).

(1) Fresh citrated blood

Freshly collected blood is the ideal medium for transfusion in haemorrhage and anaemia; it is essential in infectious and haemorrhagic states, in that it provides those elements required (complement and immune bodies) which are lost rapidly during storage. Blood for immediate use should be withdrawn, with due asepsis, into 3 per cent sodium citrate solution. Approximately 440 cubic centimetres of blood may be added to 100 cubic centimetres of sodium citrate solution. *Uses* *Collection*

(2) Stored citrated blood

The best use of stored citrated blood is in the treatment of the simple anaemia of haemorrhage. For most medical diseases fresh blood has much to commend it. For storage, 420 to 430 cubic centimetres of blood are withdrawn into an anti-coagulant solution; a widely used formula is 2 per cent disodium citrate (monohydric), 100 cubic centimetres; 15 per cent glucose, 20 cubic centimetres, (Loutit and Mollison, 1943). The blood must be agitated constantly during collection. Glucose delays haemolysis of the red corpuscles *Uses* *Collection*

1. GENERAL

62.] In principle transfusion therapy is simple, but its practice is not to be undertaken lightheartedly; the technique, apparatus and fluids used must be immaculate. In hospital a medical officer should be appointed to supervise transfusion work, and should be responsible, not only for the preparation, care and maintenance of transfusion equipment, but also for the fitness of the transfusion fluids. He must also be responsible for the blood bank if one exists. The transfusion officer is more than an expert in venepuncture—he is a specialist.

2. INDICATIONS FOR TRANSFUSION

(1) Occasion for use

Transfusion should be given only if there is a well-defined indication. Too often this valuable form of therapy is abused. In general terms a transfusion is given to restore to normal a reduced blood volume, or to provide any deficient or missing element.

(2) The effects of injury: shock, burns

One of the effects of injury to the body is a reduction of blood volume, roughly proportional to the severity of an insult, which is due to haemorrhage, externally or internally, with or without plasma loss, into the tissues. The immediate consideration in treatment is the restoration of blood volume. In burns, plasma loss into the tissues and on to the burnt surfaces reaches a high level, causing haemoconcentration, which increases the embarrassment of the circulation; blood volume should be restored with plasma or serum.

(3) Acute haemorrhage

Losses of up to 1 litre (roughly 2 pints) are well tolerated by the normal individual; greater losses cause symptoms whose severity increases in proportion to the volume lost. The purpose of transfusion in the presence of severe haemorrhage is primarily to restore blood volume, thus relieving an embarrassed circulation; the immediate restoration of haemoglobin level is of secondary importance, except in massive haemorrhages which endanger life. Blood is the ideal fluid since it will achieve both purposes; but plasma or serum can be used, post-transfusion anaemia caused by dilution being treated later.

(4) Chronic anaemia

Chronic anaemias, in general, do not need transfusion unless they fail to respond to other forms of treatment. There are obvious exceptions, for example

Mollison, 1940). They are prepared by removing the supernatant plasma from bottles in which the red cells have sedimented during storage, or which have been centrifugalized, the red-cell deposit from one bottle being added to that in another; no further diluent is needed. Such cells should be prepared as soon before use as possible; they should not be stored for more than 3 days. *Their preparation must be carried out with full aseptic precautions.* *Preparation*

(4) Liquid plasma and serum

Plasma is prepared from blood in which clotting has been prevented by the addition of sodium citrate; it therefore contains fibrinogen. Serum, prepared from clotted blood, contains no fibrinogen, but it contains about 7 per cent of protein; plasma, owing to the added citrate solution, contains about 4·5–5 per cent of protein. Both are valuable blood substitutes in emergencies, before whole blood is available or before compatibility tests have been completed. Their main use is in burns and crush injuries; they should be stored in a cool, dark place (refrigeration is unnecessary), and moved as little as possible. They are not stable products and must be inspected before use. The fluid should be crystal clear; bottles which are turbid or contain a sediment should be discarded since it is impossible to distinguish visually such bottles from those which are contaminated. *Uses* *Dangers*

(5) Dried plasma and serum

Dried plasma and serum are stable products and should be stored in a cool dark place. The dried product is reconstituted by adding pyrogen-free distilled water or isotonic glucose saline, in an amount equivalent to the original volume. Two- or four-times concentrated solutions may be prepared by adding fluid equivalent to half or one-quarter of the original volume. Once reconstituted the bottle should be used forthwith; if not used after reconstitution it should be discarded. *Storage* *Dangers*

4. APPARATUS

(1) Taking and giving apparatus

Many types of sets for the collection and giving of blood are available. The essential attribute of the apparatus, whatever its general design, is that of simplicity, so that its care and maintenance can be easily performed.

(2) Needles for collection and giving of blood

The ease with which venepuncture is performed depends largely upon the sharpness of the needle. A suitable gauge both for withdrawal and administration of blood in adults is 15/10, but gauge 19/10 or 24/10 needles are preferred by some for the collection of blood.

(3) Cleaning of apparatus

A prolific source of reactions is unclean apparatus, which forms a favourable nidus for pyrogens; therefore trouble taken to achieve perfect cleanliness is essential and will be repaid well.

(*a*) *New rubber tubing*

New tubing should be boiled for one hour in 0·1–0·2 per cent caustic soda solution; stiff wire carrying a swab or small brush should be pulled through

during storage and prolongs their survival *in vivo* after transfusion (Bushby and his co-workers, 1940; Loutit, Mollison and Young, 1943). The acid reaction of this anti-coagulant also enhances *in vivo* survival, and permits autoclaving of the mixed citrate and glucose solutions without caramelization. Immediately after collection blood should be placed in a refrigerator which is accurately regulated to 4°–6° C.; it may be used up to 21 days old. Over-cooling of the blood, especially freezing, causes haemolysis; therefore the refrigerator should be inspected periodically and a record kept of its internal temperature. Red cells older than 3 weeks should not be used since they will survive only for a short time after transfusion; the pigment released by haemolysis of older cells may, if renal function is diminished, cause anuria. Sodium citrate, 3 per cent, may be used in place of the solution given above but red-cell preservation is poor, and storage for a longer period than 7 days is not advised.

Storage

Age limit

During storage certain elements are reduced or destroyed; leucocytes disintegrate in a few hours, most of the platelets disappear in about 4 days, and prothrombin, immune bodies and complement gradually decrease.

Dangers

Blood bank

Stored blood is a potentially dangerous fluid, the sterility of which depends entirely upon meticulous attention to cleanliness, faultless asepsis, and accurate and constant refrigeration from collection until use. A blood bank should be maintained only when these desiderata are fulfilled, and should be the responsibility of an experienced medical officer.

Criteria

The fitness of stored blood can be judged only by its appearance, which on occasion may be misleading. There should be a clear-cut line of demarcation between the sedimented red cells and supernatant plasma which should be golden-yellow in colour. The clarity of the plasma is determined by its fat content. During storage, fat rises to the surface of the plasma, forming a white scum; this in itself is no contra-indication to its use. As blood ages haemolysis occurs, which is shown by a red or orange-red colour in the plasma above the cell layer; the blood may be used safely if this discoloration has not extended more than half an inch into the plasma. Stored blood in which there is more extensive discoloration should never be used. Whereas the presence of infection is disclosed usually by rapid and total haemolysis, certain coliform organisms flourish at refrigerator temperature without causing haemolysis. Transfusion of this apparently sterile blood has caused death; therefore the technique of collection and conditions of storage are of paramount importance. Only persons experienced in transfusion work should select for use blood from the bank.

Warming

Stored blood may be warmed by standing the bottle in water at 37° C. for 30 minutes. Considerable difference of opinion exists as to whether it is necessary to warm blood; on no account should it be over-heated, which would cause haemolysis. Warming has been advocated when large transfusions are to be given rapidly to an injured patient—since cold blood may cause venospasm—or to a severely ill and anaemic patient, especially if the serum of the recipient contains cold agglutinins.

(3) Concentrated red cells

Uses

Concentrated red cells are ideal for the treatment of anaemias in which the main requirement is the replacement of haemoglobin (McQuaid and

6. ROUTES AND TECHNIQUES OF ADMINISTRATION

(1) Intravenous administration

Sites and methods

A forearm vein should be selected in preference to one in the antecubital fossa especially with a restless patient, or during transport of a patient, since a needle in the antecubital fossa may be dislodged or driven through the vein, even when splinting is apparently secure, and precludes flexion of the elbow

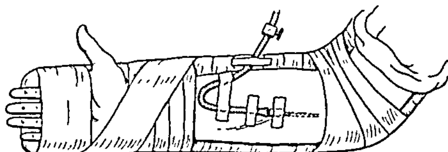


Fig. 69.—Fixation of transfusion needle. The customary position with the forearm in supination.

to the great discomfort of the patient. The forearm may be splinted in supination (*see* Fig. 69), or in pronation on a piece of Kramer wire moulded to the natural curve of the arm (*see* Fig. 70). The latter position is probably the more comfortable for prolonged transfusion. Whichever site or position is

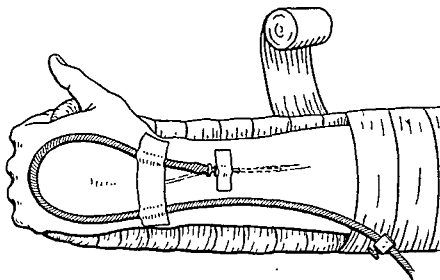


Fig. 70.—Fixation of transfusion needle. The forearm is pronated and needle inserted into a vein proximal to the wrist-joint.

Fixation of needle

chosen, about 1 inch of the needle shaft should be inserted into the lumen and the needle butt fixed by a piece of adhesive plaster placed transversely. A "U" loop of tubing should be strapped to the skin of the forearm so that any pull on it is not communicated to the needle. Skin, needle and tubing must be dry to achieve firm adhesion. Another method of fixation in prolonged

it, and then it should be reboiled in water, and cleaned in the same way as used tubing.

(*b*) *Used equipment*

Used equipment should be rinsed in cold water immediately after use, dismantled and soaked in water for several hours. Bottles and glass parts should be scrubbed with a hard brush in warm soapy water, rinsed in tap water, then in distilled water, and allowed to drain and dry. Rubber tubing should be washed through with hot water under pressure, pulled through, washed through again with water under pressure, and dried. Rubber washers and bottle caps should be cleaned in hot soapy water and dried separately. Needles should be washed with water under pressure and the bore cleaned with a stilette; after sharpening they should again be washed and dried. The inner surface of the barrel can be covered with advantage with a thin film of oil by passing a stilette dipped in liquid paraffin into the dry needle before sterilization.

(4) Sterilization of apparatus

Transfusion equipment should be autoclaved at 20 pounds pressure maintained for 20 minutes. Transfusion sets should then be dried by being placed in an oven at 120° C., or by drawing a vacuum in the autoclave. Free access of steam to the entire lumen of rubber tubing is essential. In the absence of an autoclave, bottles, glass tubing, rubber tubing and bungs can be sterilized by boiling for 5 minutes in freshly made pyrogen-free citrate or normal saline solution; haemolysis may be caused by residual water in the apparatus if it is boiled in water. Needles, if not autoclaved, are best sterilized by dry heat (160° C. for 1 hour); or in liquefied phenol, or pure lysol, rinsing well with saline before use.

5. COLLECTION OF BLOOD

Donors should be healthy young adults, who have no history of syphilis, malaria, allergic disorders, or, within the previous six months, jaundice. A vein in the antecubital fossa is selected and is congested by applying to the upper arm a sphygmomanometer cuff and inflating it to a pressure of 80 millimetres of mercury. After sterilizing the skin a small intradermal weal of local anaesthetic (0·1 cubic centimetre) is raised over the vein. The needle is inserted through the skin and into the vein in one smooth movement, about 1 inch of the shaft of the needle lying within the lumen; the needle may be held, or strapped in place with adhesive plaster. The blood flow may be augmented by the clenching and relaxing of the donor's fist: with a well-sited needle it should be unnecessary to exert suction through the air-outlet tube.

Procedure

Fainting in donors

Loss of consciousness or faintness, during, immediately after, or up to 2 hours or longer after venesection, may follow removal of a pint of blood in 2–5 per cent of donors (Poles and Boycott, 1942; Barcroft and his co-workers, 1944; Medical Research Council Subcommittee, 1944). Yawning, a feeling of warmth or vomiting are prodromal symptoms. The blood-pressure falls, the pulse is slow and thin or impalpable, the skin pale and moist; epileptiform movements may occur. Recovery is usual without active treatment, and may be accelerated by the administration of N-methyl amphetamine (Methedrine), 15–30 milligrams, intramuscularly.

hypodermic needle of appropriate gauge, the shaft of which is roughened so that the ligature grips. Another form of cannula is illustrated in Fig. 73. The trocar is removed as soon as the vein has been entered. By using this instrument "cutting down" may be avoided.

Uses

(3) Intramedullary administration

Either the site of injury (as in burns, for example) or venous spasm may prohibit the use of a vein, in which case fluids may be given into the bone marrow of the sternum in adults, (Tocantins and O'Neill, 1941; Tocantins, O'Neill and Price, 1941), or in children over 2 years of age, or of the tibia in infants, using one of the many specially designed needles (*see* Fig. 74) or a shortened intravenous or lumbar-puncture needle. Suitable needles for infants have been described by Gimson. This route is useful for the administration of prolonged transfusions.

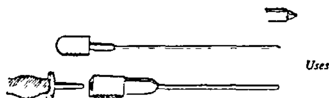


Fig. 73.—A cannula with trocar—this type avoids "cutting down".

Adults

Infants

(a) Sternum

Entry is made usually into the manubrium, but the first or second parts of the sternum may be used. About 2 cubic centimetres of local anaesthetic are infiltrated into the skin, subcutaneous tissue and periosteum. The needle, held vertically, is pushed through the outer plate, using a rotary movement. Considerable force may be required in adults, but the danger of perforating the posterior plate is slight because entry into the marrow cavity is signalled by a sudden "give" and sometimes an audible "crunch". After proving entry by the aspiration of a marrow-blood mixture, the needle is filled with citrate or saline, and the transfusion set is attached. The rate of flow is variable but is never quick; if too slow it may be aided by exerting pressure in the bottle, although this manoeuvre may cause intense pain. If the flow stops it may be restarted by shifting the needle slightly without withdrawing it, or by washing it out with

Procedure

Rate of flow

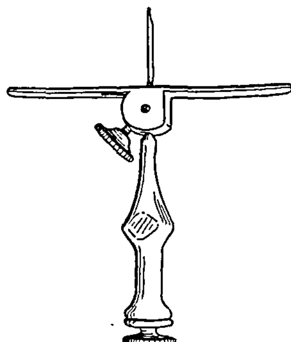


Fig. 74.—Sternal transfusion needle (M.R.C. pattern). Two malleable metal wings attached to the stop on the needle shaft, are fixed by strapping to the skin.

transfusions is to encase needle and a "U" loop of tubing in a few turns of a 4-inch plaster-of-Paris bandage (*see* Fig. 71).

Congestion of veins

A needle should be used in preference to a cannula. The following ways of congesting a vein may be useful: (i) Inflate a sphygmomanometer cuff round the upper arm and maintain the pressure well above arterial pressure for 2 to 3 minutes. Release, and inflate to a level which just fails to obliterate the radial pulse. (ii) Warm the limb with hot-water bottles. (iii) Tap the skin over

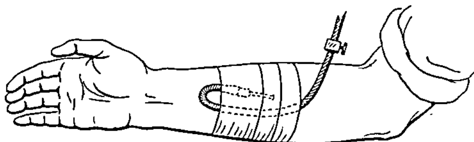


FIG. 71.—Fixation of transfusion needle, inserted into a forearm vein, with plaster-of-Paris bandage.

the vein with the finger. (iv) Alternatively clench and relax the patient's fist over a roller bandage.

Trouble taken to achieve firm fixation of the needle, together with the greatest comfort of the patient and relative freedom of local movement, will be well repaid.

(2) Cannulation

Cannulation may be necessary if no suitable vein is accessible, or if the patient is restless, or has to be transported. "Cutting down" should, whenever possible, be avoided, especially in those who are receiving multiple transfusions.

Sites

The cephalic vein, a few inches proximal to the wrist, or the great saphenous vein in the leg, lying anterior to the medial malleolus of the tibia, is selected

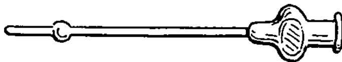


FIG. 72.—A useful type of cannula, gauge 18/10, with Record fitting.

usually. The former lies in close relation to a branch of the lateral cutaneous nerve of the forearm, whereas the latter is accompanied on its medial side by the saphenous nerve. The flow of fluids into the saphenous vein is usually slow and may have to be aided by the exertion of positive pressure in the transfusion bottle, for instance with a Higginson's syringe, attached to the air-inlet tube

An antecubital vein should never be cannulated, save in infants, since it may be required for subsequent transfusions.

A simple cannula (gauge 18/10) for adults is illustrated in Fig. 72; for small children or infants a serviceable cannula can be made from a blunted

hypodermic needle of appropriate gauge, the shaft of which is roughened so that the ligature grips. Another form of cannula is illustrated in Fig. 73. The trocar is removed as soon as the vein has been entered. By using this instrument "cutting down" may be avoided.

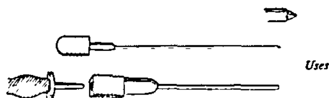


Fig. 73.—A cannula with trocar—this type avoids "cutting down".

(3) Intramedullary administration

Uses

Either the site of injury (as in burns, for example) or venous spasm may prohibit the use of a vein, in which case fluids may be given into the bone marrow of the sternum in adults, (Tocantins and O'Neill, 1941; Tocantins, O'Neill and Price, 1941), *or in children over 2 years of age*, or of the tibia in infants, using one of the many specially designed needles (*see* Fig. 74) or a shortened intravenous or lumbar-puncture needle. Suitable needles for infants have been described by Gimson. This route is useful for the administration of prolonged transfusions.

Adults

Infants

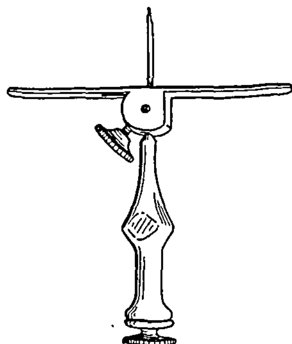


Fig. 74.—Sternal transfusion needle (M.R.C. pattern). Two malleable metal wings attached to the stop on the needle shaft, are fixed by strapping to the skin.

(*a*) *Sternum*

Entry is made usually into the manubrium, but the first or second parts of the sternum may be used. About 2 cubic centimetres of local anaesthetic are infiltrated into the skin, subcutaneous tissue and periosteum. The needle, held vertically, is pushed *through the outer plate*, using a rotary movement. Considerable force may be required in adults, but *the danger of perforating* the posterior plate is slight because entry into the marrow cavity is signalled by a sudden "give" and sometimes an audible "crunch". After proving entry by the aspiration of a marrow-blood mixture, the needle is filled with citrate or saline, and the transfusion set is attached. The rate of flow is variable but is never quick; if too slow it may be aided by *exerting pressure in the bottle*, although this manoeuvre may cause intense pain. If the flow stops it may be restarted by shifting the needle slightly without withdrawing it, or by washing it out with

Procedure

Rate of flow

citrate or saline. A fast flow, essential for the treatment of the severely injured, cannot be attained.

(b) Tibia

Procedure

The limb and thigh should be splinted along the outer side. After anaesthetizing the skin, subcutaneous tissue and periosteum, the needle is inserted into the antero-medial surface of the tibia at the level of the tibial tubercle, half-way between the anterior and postero-medial borders of the bone. The needle should be directed distally away from the epiphyseal line. The infantile tibia is easily punctured, and entry into the marrow cavity is attained usually one-eighth to three-sixteenths of an inch below the periosteum. Proof of entry and subsequent procedure are the same as in sternal puncture. The rate of transfusion, slow at first, tends to increase.

Dangers

In sternal and tibial puncture the danger of osteomyelitis, which is infrequent, may have to be considered. Mediastinitis has been reported after sternal transfusion, but this complication is rare.

(4) Control of speed of administration

A screw clamp is usually adequate, although long-maintained slow rates of flow require a more elaborate device, such as the U-tube regulator of Marriott and Kekwick (1940a). Gravity alone may be insufficient to force the fluid rapidly into the vein in those who must have a speedy transfusion, or whose veins are constricted, in which case the flow may be augmented by raising the pressure within the bottle with a Higginson's syringe attached to the air-inlet tube of the transfusion set.

Positive pressure

(5) Air embolism

Causes

The possibility of air embolism must be considered when using a pressure device to increase the rate of transfusion (Dolton, Gardner and Wylie, 1945). Pressure should be released when the bottle is three-quarters empty. Air embolism may also arise from worn rubber tubing at glass-to-rubber junctions or at the point of application of a screw-clamp. Damage to the vein wall during cannulation has been followed by fatal air embolism (Simpson, 1942).

7. VOLUME AND RATE IN TRANSFUSION

It is not possible to state dogmatically rules governing the volume and rate of transfusion. Each case is a problem in itself, and the following factors must be considered: (1) the age of the patient, (2) his general condition, (3) the state of his circulatory system, and (4) the indication for the transfusion. The young adult with a normal myocardium will tolerate the rapid infusion of large quantities of protein fluid, even when the blood volume is normal (Sharpey-Schafer and Wallace, 1942). On the other hand the anaemic patient with an enfeebled myocardium, or the patient with cardiac or respiratory disorders, must be transfused cautiously and must be constantly watched.

(1) Volume

(a) Acute injury

In the presence of severe injury or acute loss of blood, the rapid and adequate restoration of the blood is the immediate goal, and sufficient blood or plasma, or a mixture of both, to achieve this end, should be given.

(*b*) *Anaemia*

In anaemias sufficient blood, preferably freshly collected, or concentrated red cells, should be given to raise the haemoglobin to about the normal level of 14·7 grammes per cent. The amount of blood in cubic centimetres required to produce the prescribed rise in haemoglobin in adults or infants may be approximately calculated from Marriott and Kekwick's formula: *Calculation of volume*

$$\frac{\text{Percentage rise of Hb required} \times \text{patient's normal blood volume in cubic centimetres}}{100}$$

assuming that the normal blood volume is approximately 40 cubic centimetres per pound of body-weight as roughly estimated. It is emphasized that this formula does not fit every case, and that it must be used only as a rough guide to volume. Each case must be treated on its merits and its progress controlled by haemoglobin determinations. A more simple method of computing the amount in adults is to give 1 pint (568 cubic centimetres) of blood for every 10 per cent, or the concentrated red cells derived from 2 pints of blood for approximately every 15 per cent of haemoglobin rise required. These authors recommend that the transfusion should be divided into two parts, separated by an interval of 2 clear days, if the volume of whole blood needed to produce the desired rise in haemoglobin exceeds one-third of the normal blood volume; this is unnecessary when concentrated red cells are used. In infants and small children Marriott and Kekwick's formula may be used, basing the weight upon the expected weight. *Precautions* *Infants and children*

(2) Rate

(*a*) *Acute injury*

In the presence of severe injury or acute blood loss in a previously healthy patient a rate of 100 cubic centimetres per minute will be tolerated without danger up to a quantity restoring the blood-pressure to 100 millimetres of mercury. Thereafter transfusion should be pursued slowly and with circumspection.

(*b*) *Anaemia*

When a transfusion is given to overcome anaemia, the rate of administration of whole blood or concentrated red cells should not exceed 1 cubic centimetre per pound of body-weight per hour, whereas in patients with severe anaemia (haemoglobin less than 25 per cent), cachexia, or cardiac or respiratory disease, the rate should not exceed 0·5 centimetre per pound of body-weight per hour (Marriott and Kekwick, 1940b). The chosen rate of flow should be maintained accurately and steadily, and watch should be kept for signs of cardiac embarrassment; if they appear transfusion must be suspended. If these principles are followed, the circulation has time to adapt itself to the increased blood volume and to extrude the unwanted plasma, thus avoiding the increased burden which would be imposed upon the weakened myocardium in the case of a rapid transfusion. *Precautions*

8. DIRECT COMPATIBILITY TEST

The importance of the direct compatibility test cannot be over-emphasized. The details and technique are explained on p. 212.

9. TRANSFUSION IN SPECIAL CONDITIONS

(1) The effects of injury: shock

Assessment

The effects of injury are caused mainly by haemorrhage, externally, or internally into body cavities or the tissues, thus reducing the blood volume. Although the blood-pressure usually falls proportionately, and is thus a useful sign of the patient's condition when considered with the state of the pulse and his general appearance, it is sometimes well maintained in severe injury when gross blood loss is known to have occurred. Any estimates of the effects of injury must therefore include an assessment of its severity. The chief factor is the volume of tissue damaged; it may be assumed, when this equals or exceeds the volume of 2 fists (Grant, unpublished reports), as roughly estimated, that the patient's condition is serious, even if blood-pressure is normal.

Transfusion

Rate

Volume

Choice of fluids

Severe injuries

Uncontrollable haemorrhage

After first aid the immediate consideration in treatment is the restoration of blood volume and the sooner this is done after injury the better the results (Kekwick and his co-workers, 1941). Providing the circulatory and respiratory systems are normal, the transfusion should be given at a rapid rate (100 cubic centimetres per minute) until the blood-pressure has been raised to the level of 100 millimetres of mercury. With an initially satisfactory blood-pressure, the volume and the rate of the transfusion must be controlled by the clinical response of the patient. When the blood-pressure has been restored to over 100 millimetres of mercury the transfusion should be slowed down to a drip and maintained during operation, and afterwards if any untoward blood loss has occurred, or as long as risk of further bleeding persists. Blood may be used, or blood and plasma or serum in the proportion of 1:2 bottles; the pre-operative haemoglobin level should not be less than 70 per cent. It is of prime importance that blood volume be restored adequately and rapidly, and that surgical treatment follows without delay, particularly in severe injuries with gross tissue-damage, when the blood-pressure may not respond until operation has been accomplished. With internal or uncontrollable external haemorrhage transfusion should be started immediately whilst preparations are made for operation.

(2) Burns

Volume

Dangers

Anaemia

Burns are accompanied by a reduced blood volume caused by loss of plasma; haemoconcentration is present, and plasma or serum should be used. The transfusion should be started before the injury itself is attended to. The chief factor controlling the volume is the haemoglobin level, which should be kept within the normal range. Large volumes of fluid may be required, and the lungs must be watched closely, especially if the air passages have been damaged by hot air, steam or flame. Anaemia during recovery can be combated by the transfusion of whole blood.

(3) Chest injuries

Dangers

Transfusions in chest injuries should be performed cautiously since pulmonary oedema may ensue. Blood is preferable to plasma or serum, and should be administered slowly, unless serious injury elsewhere in the body demands rapid transfusion. Then the rate and the volume of the transfusion must be based upon a careful clinical assessment of the case.

(4) Head injuries

Head injuries, without free external haemorrhage or accompanying injury elsewhere, usually do not require transfusion pre-operatively. A transfusion, in the presence of a head injury, must be administered with caution. Little or no response to transfusion may be expected with spinal-cord injuries.

(5) Haemorrhage and haemorrhagic states

(a) Rh factor

Blood transfusion plays a prominent part in the treatment of ruptured uterus, ruptured ectopic gestation, premature separation of the placenta, placenta praevia, post-partum haemorrhage, and manual removal of the placenta, when accompanied by great loss of blood. As emphasized in the article Blood Transfusion: Theory, homologous blood of compatible Rh group should be used. The ABO and Rh groups of all women should be determined early in pregnancy, so that a compatible donor can be quickly selected if the need arises. *Rh factor*

(b) Gastro-intestinal haemorrhage

Patients with bleeding peptic ulcers should be transfused with blood if the haemoglobin is below 70 per cent. The belief that transfusion will cause continued or renewed bleeding is probably fallacious. If bleeding does not stop spontaneously under medical treatment, accompanied by transfusion, the latter should not be continued blindly, but should be planned to raise the haemoglobin to 70 per cent or above, and operation performed.

In persistent bleeding following tonsillectomy transfusion may be required and often will arrest haemorrhage.

(c) Haemorrhagic states

Prothrombin deficiency

A deficient prothrombin level, with a consequent tendency to bleeding rendering operation difficult, may be encountered in obstructive jaundice, biliary fistula, conditions in which there is extensive damage to the liver, polyposis, ulcerative colitis, sprue and other disorders of the gastro-intestinal tract. Vitamin K is of value, but transfusion of fresh blood may well be required to bring about immediate restoration of prothrombin, and simultaneously will improve the condition of the patient.

Essential thrombocytopenia
Platelet level

Patients with essential thrombocytopenia who are to be treated by splenectomy or ligature of the splenic artery should be transfused with fresh blood pre-operatively, to combat anaemia and raise the platelet level towards normal. Preparations for transfusion during operation should be made. It may be estimated that the transfusion of 400 cubic centimetres of blood, which is usually sufficient to control haemorrhage, will contribute to the patient's platelet count about 40,000 platelets per cubic millimetre.

Haemophilia
Haemostatic transfusion

Bleeding in haemophilia may be arrested temporarily by the transfusion of fresh blood or fluid plasma. The volume of the transfusion is not important, 100 cubic centimetres being as effective a haemostatic dose as is 500 cubic centimetres, unless it is desired to make good a haemoglobin deficiency. No matter how minor the operation to be performed upon a haemophiliac patient, a prophylactic haemostatic transfusion should be given, and preparations made for transfusion during operation.

(*d*) *Haemolytic anaemia*

Acholuric jaundice

Patients with acholuric jaundice, to be treated by splenectomy, may require transfusion before operation to improve their condition, or during operation. Freshly collected homologous group blood should be used, so that the maximal survival of the cells *in vivo* is obtained.

(6) Pre-operative and post-operative transfusion

The condition of under-nourished or anaemic patients who have to submit to operation may be improved by pre-operative transfusion. In this category are those with neoplastic disease, chronic disorders of the gastro-intestinal tract, chronic infective states and various forms of malnutrition, particularly in infants. Besides anaemia, some degree of hypoproteinaemia and dehydration may be present. Hypoproteinaemia may cause decreased gastro-intestinal motility, abnormal oedema at the site of gastro-intestinal anastomoses, predispose to pulmonary oedema and retard wound healing by inhibiting fibroblastic proliferation. Haemoglobin deficiency will also retard wound repair, and increase the dangers of anaesthesia. In such patients anaemia should be combated by blood transfusion so that the haemoglobin is raised above 70 per cent; simultaneously, plasma proteins will be increased. If operation must be performed immediately, a slow transfusion should be started before operation and continued after its completion.

Hypoproteinaemia and dehydration

Pre-operative haemoglobin level

Post-operative abdominal cases

Anaemia and hypoproteinaemia may develop post-operatively in those in whom the gastro-intestinal tract has been operated upon, and should be countered by transfusion of blood or plasma. In post-operative abdominal cases, treated with gastric suction, a pint of blood or plasma may be administered daily with advantage as a routine, so long as hydration is being performed by crystalloid solutions given intravenously.

10. CONTRA-INDICATIONS TO TRANSFUSION

(1) Absolute contra-indications

Transfusion should not be performed in those suffering from acute pulmonary oedema, myocardial failure, coronary occlusion, haemopericardium, massive pulmonary embolism or fat embolism, nor should the low blood-pressure accompanying overwhelming infections such as gas gangrene or peritonitis be combated by transfusion. In blast injury transfusion increases alveolar haemorrhage, and should be avoided unless necessitated by a severe injury elsewhere. In such a dilemma it must be performed slowly, watch being kept upon the pulmonary condition. Fat embolism should be considered in cases of fracture, particularly of long bones, and should be suspected in any injured person who develops pulmonary or cerebral symptoms without obvious cause.

(2) Relative contra-indications

Care must be exercised in the transfusion of those with myocardial or cardiac valvular lesions, pulmonary disorders such as pneumonia, severe chronic anaemia and cachexia. Transfusion of such patients must be deliberately planned according to the principles outlined above.

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BLOOD TRANSFUSION—THEORY

By JANET VAUGHAN, O.B.E., D.M., F.R.C.P.
Consulting Haematologist, Radcliffe Infirmary, Oxford

1. GENERAL

63.] The safe practice of transfusion is based upon knowledge of the principles underlying the compatibility of blood. The serological differences in blood, upon which compatibility is dependent, are constitutional; they are determined by heredity and not by environment.

2. THE BLOOD GROUPS

Differentiation The agglutinogens in human blood upon which differentiation depends can be divided into three types:

(1) ABO agglutinogens, (2) Rh agglutinogens, (3) M, N and P agglutinogens.

3. THE ABO AGGLUTINOGENS

Description It is common practice to divide human blood into four groups which depend upon the presence or absence in the cells of agglutinogens and in the serum of agglutinins of the ABO type. There are two main agglutinogens (A and B) which may occur in human red cells, or be absent therefrom, and in human

sera there are two corresponding agglutinins (anti-A or *alpha* and anti-B or *beta*), as indicated below:

Groups	*Agglutinogens in red cells*	*Agglutinins in serum*
AB	A and B	Neither
A	A	(*beta*) anti-B
B	B	(*alpha*) anti-A
O	Neither	(*alpha and beta*) anti-A and anti-B

The international nomenclature for the blood groups is used throughout the following pages. For those used to either the Moss or the Jansky classification the following key is provided :

International	*Moss*	*Jansky*
O	IV	I
A	II	II
B	III	III
AB	I	IV

(1) Principles of determination

Anti-A and Anti-B serum

Agglutination

To determine blood groups, unknown cells are tested with anti-A serum (from a group B donor) and anti-B serum (from a group A donor) containing the *alpha* and *beta* agglutinins, respectively. If agglutination occurs with both sera, the cells must contain both A and B agglutinogens and therefore belong to group AB; if agglutination occurs only with anti-A serum, the red cells contain A agglutinogen and must belong to group A; if it occurs with anti-B serum, the red cells contain B agglutinogen and belong to group B, and if it does not occur with either serum, the red cells contain neither agglutinogen and therefore belong to group O.

Types of agglutinogen

There are two types of A agglutinogen known as A_1 and A_2; the sub-group A_2 is liable to react weakly, especially when associated with B agglutinogen, therefore all anti-A grouping serum must be specially chosen to react well with cells containing A_2 and B agglutinogens (Wiener, 1943; Medical Research Council *War Memorandum* No. 9, 1943).

(2) Technical procedure of ABO group determination

Technique

The tube technique is the more accurate, but if large numbers of determinations have to be made, the tile technique is more practical (Medical Research Council *War Memorandum* No. 9, 1943).

(*a*) *Tube technique*

For tube technique 0·04 cubic centimetre of a 5 per cent suspension of red cells in sterile 3 per cent solution of sodium citrate, 0·04 cubic centimetre of serum and 0·04 cubic centimetre of sterile saline solution are delivered into a small test tube from a graduated Pasteur pipette. Unknown cells are put up in this way against both anti-A and anti-B serum and the unknown serum against known A and B cells. The tubes are shaken, capped and left at room temperature for two hours. The cap is then removed, each tube is picked up and the cell deposit dispersed by flicking with a finger. The contents of every tube which do not show undoubted agglutinates are examined microscopically.

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(b) Tile technique

In tile technique a drop of a 5 per cent suspension of red cells in 3 per cent sodium citrate solution is mixed with a drop of anti-A and anti-B serum separately on a white tile. After agitation of the tile, agglutination shows up clearly within fifteen minutes against the white background. The results must be checked by putting up the unknown serum against known cells (Medical Research Council *War Memorandum* No. 9, 1943).

(3) Sources of error

False negative or false positive results may be obtained.

(a) False negative results

False negative results may be due to: (i) use of low titre test sera, (ii) use of sera incapable of reacting with A_2 and A_2 B cells, (iii) reading the result too soon, (iv) use of infected serum.

(b) False positive results

(i) *Pseudo-agglutination* or rouleaux formation is rather stronger at high than at low temperature; it is non-specific and is prevented by dilution of the serum.

Character

(ii) *Cold agglutinins* may occur in both normal and pathological sera, which, because they act most commonly at low temperatures, are called cold agglutinins. They act rarely at room and at body temperature. Cold agglutinins may be specific or non-specific; the latter are the commoner, and are often called auto-agglutinins, since they agglutinate the cells of the person in whose serum they occur as well as other red cells. Difficulty can usually be avoided by carrying out the tests at 37° C.

(iii) *Infected cell suspensions* (the Thomsen phenomenon)

Fresh red cells or red cells which have been stored for the shortest possible time in the refrigerator should be used to prevent errors due to contaminating bacteria.

(iv) *Infected serum* will give rise to false positive results.

(4) Use of Group O blood

Whenever possible homologous group blood should be given. Group O blood should only be used in surgical emergencies. In obstetric emergencies it is preferable to employ serum or plasma, unless Rh-negative blood is available or the patient is known to be Rh positive.

(5) Direct matching test

Technique

Direct matching of the donor's cells against the recipient's serum should only be omitted when delay may endanger life. The technique of direct matching is fundamentally the same as that already described. The serum or plasma of the recipient is put up against the cells of the proposed donor. Sufficient serum or plasma can be obtained from a few drops of blood taken from the ear or with a hypodermic needle from a vein. A dilute cell suspension and a warm tile should be used to avoid false positive reactions.

(6) Biological test

A further safeguard against incompatible transfusions is the biological test in which the first 100 cubic centimetres of blood are introduced slowly, the patient being observed for untoward reactions.

4. RH AGGLUTINOGENS

Characteristics

The Rh agglutinogens are extremely complex (Murray, Race and Taylor, 1945). They differ from the ABO type since the corresponding agglutinins do not occur naturally in human serum but result from the transfusion of red cells of incompatible Rh type or from a hetero-specific pregnancy.

Occurrence

The red cells of approximately 85 per cent of English and American white subjects contain an agglutinogen of the Rh type (the term is derived from the fact that a similar agglutinogen is found in the red cells of the rhesus monkey). The remaining 15 per cent of persons, whose red cells lack the Rh agglutinogen and contain a weaker agglutinogen rh, are liable to form an agglutinin against the Rh factor if it is introduced into their circulation as when an Rh-negative person is transfused with Rh-positive cells.

Agglutinin formation

Actually, only repeated transfusions of Rh-positive blood over a period of years give rise to agglutinins. Haemolytic reactions in such people are rare, but milder reactions are not infrequent (Plaut, Barrow and Abbott, 1945). Agglutinin formation may also occur in an Rh-negative woman if she becomes pregnant with a foetus whose cells are Rh positive. More rarely the reverse takes place and an Rh-positive woman may develop agglutinins to an Rh-negative foetus (Taylor and Race, 1944). Such women run a severe risk when transfused. Further, it has been shown that the development of such antibodies in the mother is responsible for the occurrence of haemolytic disease of the new-born in the infant, and possibly for certain cases of non-specific mental deficiency.

Haemolytic disease of new-born

Infants with haemolytic disease of the new-born require immediate transfusion with Rh-negative blood (Gimson, 1944). As stated, the Rh agglutinogens and their corresponding agglutinins are extremely complex, but, in order to appreciate

TABLE

R. A. Fisher's Scheme (modified) of three linked gene loci for Rh with genes, agglutinogens and agglutinins

		Agglutinins and their reactions					
Agglutinogen present	Genes present	Anti-Rh' Anti-C	Anti-Hr (st) Anti-c	Anti-Rh_0 Anti-D	Anti-Rh'' Anti-E	Anti-d	Anti-e
Rh_z	CDE	+	−	+	+	(−)	−
Rh_1	CDe	+	−	+	−	(−)	+
Rh_y	CdE	(+)	(−)	(−)	(+)	(+)	(−)
Rh'	Cde	+	−	−	−	(+)	+
Rh_2	cDE	−	+	+	+	(−)	−
Rh_0	cDe	−	+	+	−	(−)	+
Rh''	cdE	−	+	−	+	(+)	−
rh	cde	−	+	−	−	(+)	+

The brackets indicate that, though prophesied, the reactions have not yet been confirmed serologically.

certain apparently anomalous reactions, it is helpful to have available the scheme for the arrangement of the three linked gene loci, suggested by Fisher, to be characteristic of each agglutinin (Race, 1944). *See* Table, p. 213.

The method of action of the simpler-known pathological sera is made apparent from a study of these linked genes. Thus, anti-Rh' or anti-C reacts with each agglutinogen containing the C gene and anti-Hr or anti-c reacts with each agglutinogen containing the c gene etc. The commonest serum found is anti-Rh_0 (anti-D). In addition to the five known sera shown in the Table there are two others which are found in practice, (i) anti-Rh_1 which contains both anti-Rh_0 (anti-D) and anti-Rh' (anti-C) and (ii) anti-Rh_2 which contains both anti-Rh_0 (anti-D) and anti-Rh'' (anti-E). In practice the three sera which serve to distinguish the more common agglutinogens are anti-Rh_0 (anti-D), anti-Rh' (anti-C) and anti-Rh'' (anti-E). Anti-C reacts with 70 per cent of Rh-positive cells, anti-E reacts with 30 per cent of Rh-positive cells, and anti-D reacts with 85 per cent of Rh-positive cells.

Rh agglutinins are of two types, one known as complete, the other as incomplete or blocking (Race, 1944). The complete agglutinin causes agglutination in the normal way when put up against suitable Rh-positive cells suspended in normal saline solution at 37° C. The incomplete or blocking agglutinin is absorbed by the Rh-positive cells suspended in saline but fails to cause agglutination. It prevents, however, the subsequent agglutination of the cells by known complete agglutinin if this is added. The incomplete agglutinin is, however, effective in agglutinating red cells suspended in human plasma or serum, or human or bovine albumin. Both complete and incomplete agglutinins may be present in the same serum. Unrecognized incomplete agglutinins probably explain those cases of erythroblastosis in which it is stated that no agglutinins are present in the mother's serum.

Practical suggestions

The following practical suggestions are made: (i) Rh typing should, if possible, be carried out in all individuals who receive repeated transfusions, and only blood of a correct Rh group be given; (ii) Rh typing should be performed for pregnant women who give a history of repeated miscarriage or stillbirth, or suggestive of haemolytic disease of the new-born in previous infants; (iii) Rh-negative blood should be available in blood banks for the following: (a) infants with haemolytic disease of the new-born, (b) obstetric emergencies, (c) women with suggestive histories of repeated miscarriage or stillbirth, (d) women whom antenatal typing has shown to be Rh negative.

If transfusions are required when Rh-typing serum and skilled personnel are not available the red cells of the proposed donor diluted with normal saline solution should be incubated for two hours with the serum of the recipient at 37° C. and the deposit should be then examined microscopically for agglutination.

Technique of Rh typing

Correct Rh typing can only be carried out by people with considerable experience and knowledge because of the complexity of the Rh agglutinogens and agglutinins (Boorman, Dodd and Mollison, 1942; Race, 1944). At least three different sera, which are only obtainable at present from women who have had children with haemolytic disease, are needed. It is therefore impracticable, though desirable, to Rh type all pregnant women.

5. THE M, N AND P AGGLUTINOGENS

M and N agglutinogens occur in all human red cells but so rarely produce agglutinins that they are without practical significance in considering transfusion. P agglutinogen is rarely found in red cells and even more rarely causes agglutinin formation.

6. ATYPICAL AGGLUTININS

It appears likely that with a more careful technique many other agglutinogens and agglutinins will be recognized. One patient has recently been described who developed three hitherto unrecognized agglutinins following transfusion with the blood of eight donors (Callender, Race and Paykoc, 1945).

7. TRANSFUSION REACTIONS

Reactions following transfusion may be of four types: (1) pyrexial, (2) haemolytic, (3) circulatory, (4) delayed.

(1) Pyrexial reactions

Character

Pyrexial reactions which are usually extremely mild occurring during or immediately after a transfusion with blood or blood products are reported in about 6 per cent of patients transfused. Patients with ulcerative colitis and severe anaemia show a considerably higher reaction rate.

Cause

A slight rise in temperature, rigor and headache are most common; these symptoms are also seen with incompatible transfusions. Pain in the loins, vomiting and urticaria are all recorded. An alarming anaphylactic-like reaction may occur. The cause of such reaction is often obscure. Known factors are dirty apparatus, infected blood, haemolysed blood due to overheating, incompatible blood due to faulty ABO or Rh grouping and too rapid a rate of administration. The operative factor is sometimes in the patient rather than in the fluid administered.

Treatment

The usual treatment is to slow the rate. The patient should be reassured and kept warm and comfortable. If pain in the loins is acute, the transfusion should be stopped and alkali administered. If the reaction is anaphylactic in character, adrenaline is useful.

(2) Haemolytic reactions

Cause

Haemolytic reactions may result from: (1) the transfusion of blood of incompatible ABO or Rh type; (2) the transfusion of blood previously haemolysed by infection or overheating. After 10 to 100 cubic centimetres have been given the patient usually, but not invariably, complains of sudden severe lumbar pain.

Character

In rare instances the patient dies within a few hours; more commonly oliguria develops, followed sometimes by complete anuria. The urine contains methaemoglobin, haemoglobin and often casts, while methaemalbumin, increased bilirubin and a rising urea are found in the plasma. Death may occur in from six to eight days from renal failure. In other cases there is a sudden increase in urinary flow about the sixth to eighth day with complete recovery.

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(3) Differential diagnosis

It is important to determine the cause of a severe reaction. In addition to checking the group of both donor and patient, two laboratory tests are valuable: (1) If the blood given is incompatible as regards the ABO system a high titre of iso-agglutinins develops in the blood of the recipient, reaching a maximum between the fifth and twentieth day. Anti-Rh agglutinins only develop after repeated transfusions (Boorman, Dodd and Mollison, 1945). (2) The transfused cells are rapidly eliminated following the transfusion of incompatible blood even though no haemolytic reaction is apparent. An unsatisfactory haemoglobin level following transfusion may be indicative of the use of incompatible blood.

Iso-agglutinins

Cell survival

(a) *Treatment*

Alkali

Glucose

Operative

The urine should be kept alkaline. This may be done by the administration of sodium bicarbonate by mouth (Bushby and his co-workers, 1940) or by the intravenous administration of one litre of sodium lactate solution 2 grammes per 100 cubic centimetres or 1 pint of 3–4 per cent sodium citrate, followed by a slow drip of glucose. Fluids should not be forced after the urine has once become alkaline (Maegraith, Havard and Parsons, 1945). Splanchnic block and decapsulation of the kidney have proved disappointing.

(b) *Pathology*

The appearance of the kidney at necropsy is similar to that seen in a variety of conditions associated with anuria (Maegraith, Havard and Parsons, 1945). The view that anuria is dependent upon blockage of the tubules with pigment is no longer generally accepted.

(4) Circulatory failure

Death may result occasionally from overloading of the circulation by too rapid administration of transfusion fluids, particularly in elderly and severely anaemic patients (Drummond, 1943).

(5) Delayed reactions

Incidence

Cause

Available evidence suggests that 10 per cent of patients receiving transfusions of serum or plasma develop mild jaundice 40–140 days later. Instances of acute hepatic necrosis with death have occurred also. There is no evidence to prove that jaundice follows transfusion of whole blood. The pathology of homologous-serum jaundice is indistinguishable from that of infective hepatitis (Dible, McMichael and Sherlock, 1943). The aetiology is still obscure.

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BOILS, CARBUNCLES, FURUNCULOSIS

By CHARLES DONALD, O.B.E., Ch.M., F.R.C.S.
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1. DEFINITIONS

Boil 64.] A boil is a localized, superficial, inflammatory swelling following upon the staphylococcal infection of a hair follicle. The condition may resolve or pass on to abscess formation.

Carbuncle A carbuncle is a staphylococcal infection of the skin and subcutaneous fat, originating in a hair follicle, thence spreading to the subcutaneous fat and, by further extension in that layer, infecting other hair follicles. There is necrosis of the subcutaneous tissue and usually also of some of the overlying skin.

Furunculosis Furunculosis is a condition of recurrent boil formation over a period of time. While the boils may exist as a diffuse crop, more usually there is simply the recurrence of a single boil in the same region as that previously affected, although there may be adjacent traces of others which are fading or in an incipient stage of activity.

2. AETIOLOGY

Factors which may be concerned in the production of boils and carbuncles are lack of cleanliness, mechanical irritation and such debilitating diseases as diabetes, nephritis, blood diseases and chronic alcoholism, but a lessened resistance to staphylococcal infection would seem often to be the only explanation.

An explanation (Price, 1944) of furunculosis has been advanced in which skin bacteria are classified as either residents or transients. The latter, the ordinary pathogenic bacteria, are but loosely attached and are easily removed and killed. The former, organisms of low pathogenicity, are much more ingrained and difficult of removal.

It is thought that discharges from the initial boil may spill pathogenic organisms, which, under conditions not understood, may become residents, and, in the course of time, becoming rubbed into a hair follicle, may produce further furuncles, the process being cumulative.

3. MORBID ANATOMY

Boils In a boil (Fig. 75) the early inflammation may recede and the condition subside spontaneously—a blind boil—or it may progress to form an abscess, in the centre of which is a slough or core. The surface eventually breaks and the slough and pus are discharged. The condition then resolves.

Carbuncles In a carbuncle (Fig. 76) the infection in a hair follicle is not circumscribed at an early stage, as in a boil, and, passing down the adjacent columna adiposa, it reaches the subcutaneous fat. In this, aided by a spreading thrombosis of small vessels, it spreads until it becomes limited by inflammatory reaction in tissues not devitalized by thrombosis. The extent of spread is greatly variable depending upon the resistance of the patient. Spreading roughly concentrically, the infection in the subcutaneous fat passes up other columnae adiposae to infect other hair follicles and surface glands.

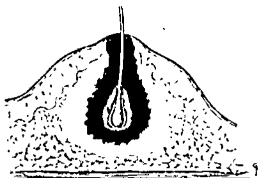


Fig. 75.—Cross section of boil just before eruption (diagrammatic).

At the orifices of these there occur discharges of pus, so that the surface appearance resembles in miniature the nozzle of a watering-can; but the vessels to the skin involved may also become thrombosed, and are pressed upon by the swelling, so that, particularly in the centre, there is some death of tissue. This necrotic tissue separates gradually from the underlying granulation tissue which forms as a limiting reactive barrier. There is not much liquid pus formation. The granulation tissue is at first dirty-yellow-looking because of some still-remaining slough, but gradually throws this off to show in its usual bright red colour.



Fig. 76.—Cross section of discharging carbuncle (diagrammatic).

In a large carbuncle the necrotic process is patchy and islets of intact epithelium are left. These are usually sufficient to provide a covering to the bare areas by their proliferation.

The carbuncular process may be small, little larger than a boil, or it may be six inches or more in diameter, spreading in the neck sometimes from ear to ear.

Spread of infection Boils and carbuncles give rise sometimes to further spread of infection. Cellulitis, lymphangitis and lymphadenitis are not uncommon but usually subside with or before the causative condition itself. Of more serious import, however, and this naturally tends to occur more frequently in patients debilitated by other disease, the thrombosed veins in the base of a carbuncle

BOILS, CARBUNCLES, FURUNCULOSIS

By CHARLES DONALD, O.B.E., Ch.M., F.R.C.S.
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1. DEFINITIONS

Boil

64.] A boil is a localized, superficial, inflammatory swelling following upon the staphylococcal infection of a hair follicle. The condition may resolve or pass on to abscess formation.

Carbuncle

A carbuncle is a staphylococcal infection of the skin and subcutaneous fat, originating in a hair follicle, thence spreading to the subcutaneous fat and, by further extension in that layer, infecting other hair follicles. There is necrosis of the subcutaneous tissue and usually also of some of the overlying skin.

Furunculosis

Furunculosis is a condition of recurrent boil formation over a period of time. While the boils may exist as a diffuse crop, more usually there is simply the recurrence of a single boil in the same region as that previously affected, although there may be adjacent traces of others which are fading or in an incipient stage of activity.

2. AETIOLOGY

Factors which may be concerned in the production of boils and carbuncles are lack of cleanliness, mechanical irritation and such debilitating diseases as diabetes, nephritis, blood diseases and chronic alcoholism, but a lessened resistance to staphylococcal infection would seem often to be the only explanation.

An explanation (Price, 1944) of furunculosis has been advanced in which skin bacteria are classified as either residents or transients. The latter, the ordinary pathogenic bacteria, are but loosely attached and are easily removed and killed. The former, organisms of low pathogenicity, are much more ingrained and difficult of removal.

It is thought that discharges from the initial boil may spill pathogenic organisms, which, under conditions not understood, may become residents, and, in the course of time, becoming rubbed into a hair follicle, may produce further furuncles, the process being cumulative.

Furunculosis usually disappears in a variable time, which may be several years, as the patient recovers his resistance to staphylococcal infection.

Carbuncles, however, are associated with a definite mortality rate which it is impossible to give with accuracy, since only the more severe cases come to hospital. Death occurs from pyaemia or from exhaustion in patients already debilitated by some general disease. Excluding patients suffering from general constitutional diseases, there is a mortality rate of about 2 per cent in patients with carbuncle admitted to hospital, the causes being septicaemia, pyaemia and cavernous sinus thrombosis.

6. TREATMENT

(1) Preventive

Sufferers from boils may to some extent help to prevent their spread by scrupulous cleanliness and by the avoidance of irritation in the area liable to attack. Assistance in these may be got from shaving such areas and from the use of a fine dusting powder. The application of one per cent cetyltrimethyl ammonium bromide (Ctab or Cetavlon), the area being swabbed over with solution, reduces the number of skin bacteria to a very low figure, and this solution may be used with advantage.

Patients suffering from furunculosis can do little beyond this apart from general measures of hygiene. The use of autogenous vaccines seems to be followed by success in a moderate proportion of cases. Staphylococcal toxoids are still on trial.

Sufferers from diabetes, nephritis and other debilitating diseases particularly require to pay attention to cleanliness and avoidance of irritation, in addition to the specific medical measures directed towards their ailment.

Treatment of severer forms

In the treatment of the severer forms of these infections the patient should be made to drink copiously except when the clinical state is so debilitated that excessive fluid intake might aggravate or precipitate a hypostatic pneumonia.

(2) Non-operative versus operative treatment

Excision

The tendency in the past ten or fifteen years has been towards conservative, non-operative methods of treatment. The argument has not reached finality, but it is fair to say that most surgeons favour non-operative methods in the great majority of cases, with the reservation of operative interference to a few instances, and then usually at a mature stage in the condition. There is, however, a school of thought which advocates the total excision of carbuncles when such a course is possible. The underlying argument is that excision allows of greater comfort from the beginning, that it prevents debility from septic absorption, and that it removes the risk of pyaemia. The non-interventionists claim equally good results from conservative methods, and, since most fatalities occur in the cases complicating other diseases, argue that an anaesthetic and operation only further endanger life. There is, however, almost complete agreement that there should be no operative intervention in lesions, boils or carbuncles on the dangerous area of the face and in the nostrils. Thrombosis of the cavernous sinus seems undoubtedly to have a connexion with incisions here, although an incision at a very late stage when the condition is well walled off would probably not lead to any harm. An incision

give off small infective emboli, to give rise to pyaemia. These emboli may pass to the kidney, where, after lodging under the capsule, they erupt into the surrounding fat and give rise to a perinephric abscess. Rarely they lodge in the brain, causing cerebral abscess, or in the myocardium whence the pericardium may be infected.

On the face, in the "dangerous area" bounded by the upper lip below, by the eyes and root of the nose above, and by lines drawn from the outer canthus to the angles of the mouth, a boil or carbuncle may cause thrombosis affecting either the angular vein or the pterygoid plexus of veins. Both of these, the former through its connexion with the superior ophthalmic vein at the inner angle of the orbit, communicate with the cavernous sinus. The infective cavernous sinus thrombosis so caused is commonly fatal.

4. CLINICAL PICTURE AND DIAGNOSIS

Boil

A boil, until it starts to resolve spontaneously or until it starts to discharge, becomes progressively more tender to the touch. Actual pain is usually moderate, although in some situations, as in the external auditory meatus and in the nose, it may be severe. Constitutional symptoms are slight.

Carbuncle

A carbuncle is easily recognized when it is large. Smaller ones, such as those occurring on the dorsum of the proximal phalanges of the fingers, are frequently mistaken for boils. Starting as a small red area on the skin, with swelling of the surrounding superficial tissues, the redness and general swelling becomes more diffuse concentrically or in some directions more than others. As the inflammatory process in the subcutaneous fat extends, the most *central part becomes bluey-red and soft; at the periphery is hard* indurated reactionary swelling. In the centre, at the mouths of hair follicles, yellow spots appear and discharge a little pus. As the process gets more severe this central area sloughs irregularly and incompletely.

The reparative processes may be going on at one side of a carbuncle while at the other extremity it is still spreading.

When the slough has separated, a floor of healthy granulation tissue is left. The skin gradually and quickly grows in from the edges to cover large bare areas.

Carbuncle formation is accompanied by severe pain until separation of the slough begins and the tension is lessened. There is usually a good deal of constitutional disturbance and the temperature and pulse are raised.

Diagnosis

The diagnosis of boils and carbuncles presents little difficulty. When a black necrotic centre is a marked feature the possibility of the infection being cutaneous anthrax should be thought of. The malignant pustule of cutaneous anthrax occurs most commonly on the face, hands and fingers. The pustule discharges blood rather than pus, the black necrotic centre is surrounded by vesicles from which the anthrax bacilli can be recovered, and there is surrounding oedema rather than induration.

In a carbuncle, and when boils keep recurring, the urine should always be examined for sugar and for evidences of nephritis.

5. PROGNOSIS

Boils very rarely give rise to illness endangering life or causing death. Occasionally cavernous sinus thrombosis is initiated by a nasal furuncle.

compress to maintain the heat, and, by bandaging, to immobilize the part as much as possible. For instance, in a large carbuncle of the neck the neck ought to be kept rigid, and the head supported, by a broad figure-of-eight flannel bandage passed round the neck and brow and under both armpits.

As soon as it is obvious that the process is subsiding, dry gauze, still fluffed-up, should be substituted for the hot compress. This lessens the risk of surrounding contamination.

Facial

In facial and nostril cases some modification is necessary since large compresses cannot be comfortably applied. A satisfactory method is for the patient to hold a large wad of cotton-wool, soaked in hypertonic salt solution, to the areas affected, repeatedly refreshing the heat by re-immersion of the wool in the solution contained in a vessel in front of him. This is done for some twenty minutes every four hours, the rather inadequate compress which is practicable being applied in the intervals. In carbuncle of the upper lip the patient may lean over to hold the lip into the top of a wide jug filled with the solution.

Upper limbs

For carbuncles and boils on the upper limbs an arm bath filled with hypertonic salt solution may be similarly used as in other infective inflammatory conditions.

Prevention of further infection

Once a boil or carbuncle has erupted, measures should be taken, especially in those liable to staphylococcal infections, to prevent the spilled pus causing further infection around. This may be done mechanically by strips of adhesive plaster applied to the surrounding shaved skin. This, however, is sometimes damaging to skin. Otherwise, if heat is not still being applied, pieces of lint soaked in alcohol may be applied around, or, if heat is still being applied, the area is carefully cleaned with Ctab at each removal of the dressing. Penicillin cream may be applied to the surrounding area on the same rationale.

(4) Chemotherapy

The conditions being essentially staphylococcal, sulphathiazole or sulphadiazine are the most beneficial of the sulphonamide type of drugs. In the great majority of cases, naturally, there is no need for their administration, their depressant effects not being warranted, but in infections of the face or when the local condition is more severe than usual, or when there are complications such as pyaemia, then they or penicillin should be given in adequate doses. The local application of sulphonamide powders probably has little or no effect; systemic sulphonamides will help to keep the infection local.

Effect of penicillin

The effect of penicillin in these staphylococcal infections has yet to be fully determined, although, as with the sulphonamides, it is assumed that it will usually limit systemic spread of the infection, and will deal with a staphylococcal septicaemia from these causes as from others. Local success, in respect of quicker subsidence of carbuncle or furuncles, is being widely claimed following systemic administration of the drug; such a laudable result, however, in furunculosis does not seem to be followed by immunity against further crops for any considerable length of time. The value of local penicillin applications of various types has still to be accurately assessed. Penicillin will therefore be given on the same indications as those for sulphonamides, when the local condition is severe, when the lesion is in a dangerous area, and when systemic invasion has occurred.

at this stage, however, can only be justified when the skin pellicle overlying any localized pus is unusually slow in disrupting.

Ligature of the angular vein at the side of the nose near the inner canthus is advocated by some as a precautionary measure against cavernous sinus thrombosis in facial infections. The arguments against this are heavy. Such extensions are rare and facial infections common. That actual thrombosis is occurring is difficult to determine. The angular vein may be collapsed and difficult to find; the little incision may later be disfiguring. The equally available route for the infection to reach the sinus by the pterygoid plexus is unaffected. More often the procedure is done when the facial infection is extending towards the canthus, and it would seem then to carry the risk of precipitating thrombosis and subsequent disaster rather than its prevention.

Penicillin

With the advent of penicillin it is unlikely that the procedure will be so much advocated in the future, save possibly in such a case as might be imagined more than encountered, in which there is recurrent thrombosis and embolism imperfectly controlled by the chemotherapy.

(3) Non-operative methods of treatment

Small boils which are not causing acute discomfort to the patient may be dealt with by local protection and immobilization of the area by the application of strips of adhesive strapping over and around the boil. When the boil has burst, as will be seen by soiling of the strapping, the strip over the boil is removed and replaced by another strip with a hole in it to allow the escape of the discharge and prevent its infecting adjacent hair follicles.

Application of heat

Such a method is usually employed only to allow the patient to go about his work without the inconvenience of other forms of treatment. Heat, in one form or another, is the most indicated early treatment, to promote hyperaemia and to relieve pain. Heat may be applied in the form of fomentations, compresses, cataplasms, baths and radiant heat. Some of the solutions employed in compresses, pastes and baths are hypertonic. The rationale of their use is that, when the skin is intact they draw toward the surface the exuded fluid which is raising the tension and impeding the bloodflow in the subcutaneous tissue. When the skin has broken their use helps in the quick separation of the core and detritus.

Fomentations

Ordinary hypertonic salt solution, one ounce to the pint (half an ounce to the pint in facial cases), may be used as a hot compress applied four-hourly. Another commonly used solution is made of saturated magnesium sulphate solution 40 parts, glycerin 10 parts, boiling water 30 parts. Alternatively, 12 per cent sodium sulphate may be employed. Boric fomentations are permissible only if they are well wrung-out and changed as soon as they are cool. They must not be left as damp, cool dressings.

Compresses and fomentations should always be very much larger than the carbuncle or boil. They are often made much too small. If they are to promote a real hyperaemia they must extend far beyond the limits of the inflammation. Compresses are best made of fluffed-up gauze wrung out of a boiling solution. When the skin has broken, the fluffing allows of the interstices of the gauze reaching into the crannies of the lesion and, when removed, bringing away much of the detritus.

It is important both to put sufficient wool and jaconet covering above the

compress to maintain the heat, and, by bandaging, to immobilize the part as much as possible. For instance, in a large carbuncle of the neck the neck ought to be kept rigid, and the head supported, by a broad figure-of-eight flannel bandage passed round the neck and brow and under both armpits.

As soon as it is obvious that the process is subsiding, dry gauze, still fluffed-up, should be substituted for the hot compress. This lessens the risk of surrounding contamination.

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(5) Operative methods

Excision of a carbuncle is skin-consuming and should not be made to include all the induration around. A short course of chemotherapy should be given coincidently.

Incisions

Incisions, when employed, should not be made prematurely. In a boil, a simple incision when the thin yellow tissue over the core is not giving way quickly, and there is marked pain and tenderness, will suffice to give ease, especially if the part be bathed immediately thereafter. The incision should not go beyond the inflamed area. In a carbuncle a crucial incision is made. The flaps so formed are undermined by cutting so that the columnae adiposae are cut across. The cavity so made is then lightly packed with fluffed gauze impregnated with the hot solutions or pastes already mentioned under non-operative treatment.

Some surgeons prefer to use the diathermy knife in making these incisions. As has been already noted there is almost unanimous agreement as to the undesirability of incisions in facial and nasal infections.

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[References to other titles are given under Boils, Carbuncles, Furunculosis in the Index Volume. The subject of Boils, Carbuncles, Furunculosis is also dealt with under the heading of Boils and Carbuncles in the *British Encyclopaedia of Medical Practice* (1936), Vol. 2, p. 547.]

BOIL, DELHI

See SURGERY IN THE TROPICS

BONE GRAFTING

By B. H. BURNS, F.R.C.S.

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1. GENERAL

(1) Historical

65.] The first bone graft on a human being was done by Macewen of Glasgow in 1880. The patient was a boy who two years previously had suffered from osteomyelitis resulting in the loss of some 5 inches of the shaft of the humerus.

Macewen collected five wedge-shaped pieces of bone from the tibias of patients on whom he had performed osteotomy. These were used to fill the defect in the humerus which subsequently developed into a bone differing but slightly from the normal.

The impulse, however, which has given bone grafting its present extended use came not from Macewen's initial success but from another operation altogether. It came from the introduction by Lane in 1894 of the operative treatment of fractures. Dissatisfied as he was with Lane's metallic internal splints, Albee (1930, 1940) in 1911 initiated the employment of living bone grafts as internal splints.

(2) Purpose of grafting

Healing *Bridging* *Arthrodesis*

The purposes for which bone is now transplanted are, broadly speaking, to promote the healing of ununited fractures; to bridge defects resulting from injury, from osteomyelitis or from non-malignant tumours and cysts of bone; and to cause artificial ankylosis of joints (arthrodesis).

The graft has two functions. First it is a method of internal splintage, and secondly it is a source or scaffolding from or by which new bone can be formed.

(3) Type of bone

Live autogenous bone

With very few exceptions bone grafting implies the use of live autogenous bone. There is much experimental evidence to show that live bone has a greater capacity for bone formation than has dead bone; but dead autogenous bone can be effective, as is shown by the success of grafts which have been boiled after accidental contamination.

Heterogenous bone

The use of heterogenous bone in the form of os purum, or specially prepared boiled beef bone introduced by Orell in 1934, has not become popular. It has not the same bone-forming qualities as has autogenous bone.

Homogenous bone

Homogenous bone has occasional uses; for instance for a child with congenital pseudarthrosis of the tibia, bone can be successfully borrowed from the tibia of the mother. Further, bone from a donor of a different blood group can apparently be used with safety (De Forest Smith, 1937, 1941). The existence of "bone groups" has not been shown.

(4) Fate of graft

Death

The fate of the graft immediately after transplantation is uncertain. Whether it dies entirely or whether it is from the start actively osteogenic through its osteoblasts has been a matter of dispute. It seems probable that some of the cells of the graft may survive throughout but that most of its cellular elements die.

Regeneration

Thus to a large degree the graft becomes regenerated by the invasion of blood-vessels and blood cells from the host. By this process, called by Barth "creeping substitution", the graft eventually becomes completely incorporated in the host.

(5) Source of graft

Tibia

The tibia provides particularly suitable grafts for use in long bones when internal splintage is a main function. The graft is taken from the subcutaneous surface and considerable strength and width may be obtained.

When an especially wide graft is required the anterior border is included. To obtain an especially bulky strut for his ischio-femoral arthrodesis Brittain (1942) takes even the whole of the subcutaneous surface, including both borders. There is no advantage in taking the periosteum with the graft (Pollock and Henderson, 1940). (*See* Fig. 77.)



FIG. 77.—Cross section of tibia showing cutting of grafts of various sizes. The first illustration demonstrates usual size of graft, the second the amount required for an especially wide graft, and the third the amount used for ischio-femoral arthrodesis. (*Brittain.*)

Other common sources of bone for grafting are the crest of the ilium, the shaft of the fibula and the ribs. *Other sources*

The ilium is more successful in the early production of new bone than is the cortex of the tibia. As it is composed of cancellous bone it is more readily accessible to the ingrowth of new blood-vessels and cells. *Ilium*

(6) Principles of applying the graft

Whatever the type of graft used and whether for ununited fracture or for arthrodesis, its use should be governed by the following principles.

(a) There should be the largest possible area of contact between the graft and the host bone. *Area of contact*

(b) There must be firm and prolonged fixation. *Fixation*

Another factor of importance is that the graft should lie comfortably in its bed without tension. The persistence of bending stress may result in fracture

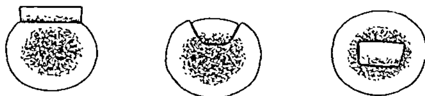


FIG. 78.—Diagram of cross section of bone showing, from left to right, onlay graft, inlay graft and intramedullary graft.

or absorption of the graft. The only stress that the graft should be exposed to is a compression force.

(7) Types of graft

The two types of graft most commonly used are the *onlay* graft, which was introduced in 1921 by Henderson (1940), and by Campbell (1932, 1939), and the classical *inlay* graft of Albee. (*See* Fig. 78.)

(*a*) *The onlay graft*

In this type, a long bulky plate of autogenous bone is applied to a prepared surface on the host bone. After scar tissue has been excised between the *Bone plate*

Receiving surface ends of the fragments and they have been freshened, the receiving surface of the bone is flattened to the required width with a chisel. The flattening does not open the medulla, the cortex remaining intact to give a firmer bed to the graft. *Fitting* The graft is then accurately fitted to the prepared surface, where it is held by bone clamps whilst screws are inserted. Bone chips may be used to fill up crevices. Chips or shavings obtained in preparing the graft bed are convenient.

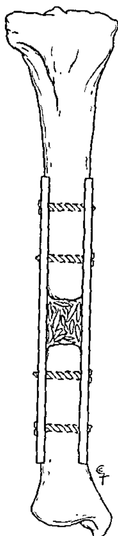


FIG. 79.—The double onlay graft.

(*b*) *The double onlay graft*

This is an extension of the principle of the onlay graft and is used in conditions in which union is especially difficult to achieve, as in bridging a gap. *Bridging* Two strong grafts are placed one on each side of the host bone. These are held in position by long screws or bolts, each running right through the host bone and both grafts. If a gap is bridged the normal thickness of the bone is restored by adding bone chips or larger pieces to the two main struts.

Advantage This method has a particular advantage when the host bone is of poor quality and incapable of giving a firm hold to the screws. (*See* Fig. 79.)

(*c*) *The inlay graft*

In this type the graft is not superimposed on the cortex, as in the onlay, but is sunk into a gutter. *Preparation of bed* A bed is prepared by removing a length of the cortex on each side of the fracture. *Wedge-shaped graft* The sides of the bed are made to slope inwards in the form of a wedge the point of which is towards the medullary canal. The graft is cut at the same angle so that it is wider at its periosteal than at its medullary surface. The graft is then placed in the gutter and is driven down with a punch so that the sides are held firmly by the host. *Fixation* Screws are driven through the graft and through the cortex of the bone on the opposite side. This gives firm and lasting fixation.

(*d*) *The sliding inlay graft*

In this modification of the inlay the graft is obtained from the fractured bone and thus the necessity of borrowing from another bone is avoided. *Preparation of bed* The gutter is prepared in a manner similar to that for the inlay graft but it is twice as long on the one side of the fracture as on the other. The pieces of bone removed from the gutter are used as grafts and their position is changed, *Long and short grafts* the longer fragment being placed across the fracture and the smaller fragment being used to fill the remaining gap (*see* Fig. 80). If required the smaller fragment can be used to double the main graft at the fracture site. *Fixation* The main fragment is fixed by four screws.

(*e*) *The intramedullary graft*

The graft is inserted into the medullary cavity of each fragment (*see* Fig. 78). *Difficulty and disadvantage* It is technically difficult to insert a sufficient length of graft and often secure fixation is not obtained. The method also has the disadvantage of

blocking the medullary cavity and so may dam up an important source of new bone.

(f) The osteoperiosteal graft

This is a thin and flexible graft chiselled from the cortex of the tibia and containing periosteum and a thin layer of cortex. Its use depends upon the fact that the deeper or cambium layer of the periosteum has some osteogenic power. Although this type of graft may promote bone formation satisfactorily in the young, in whom the cambium layer is thicker, its powers are much diminished in older people and it does not provide any fixation. It is suitable for cranioplasties and is sometimes used for spinal grafts. *Flexible graft* *In young and old*

(8) Method of fixation

Whichever type of graft is used fixation is best obtained by screwing the graft to the bone with vitallium screws. When fixation relies on joinery alone as was the custom until recently, the graft is apt to work loose, for no matter how firm the impaction at time of operation the slight absorption which takes place at the area of contact will lead to a loosening of the graft during the second, third or fourth week. Fixation by wire or by other sutures should be avoided because the encirclement of the bone is likely to impair its blood supply. Formerly there was, very properly, a prejudice against using any form of metallic fixation. The metals used were not suitable as they caused irritation and rarefaction of the bone and consequently often became loose. With the introduction of vitallium, however, which is completely inert in bone, this objection has disappeared. *Vitallium screws* *Danger of other methods*

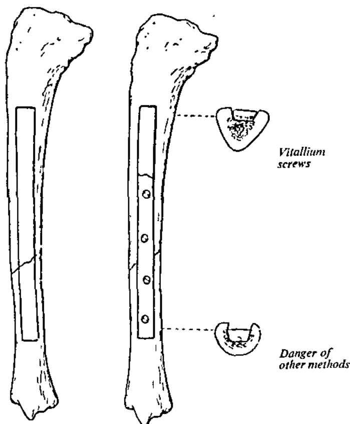


Fig. 80.—The sliding inlay graft. The first illustration shows the graft cut; the second shows the graft slid across the fracture and screwed into place.

The most generally useful type of screw is the machine screw, self-tapping and completely threaded. The standard Sherman screw is ideal. It should be inserted into a hole made by a drill of the same diameter as the root diameter of the screw. The drill holes are more accurately made by a motor drill than by a hand drill. The screws can be made to enter more easily if the proximal part of the hole is enlarged by a reamer and their insertion is greatly facilitated by the use of a screw-holding screwdriver. *Technique*

2. THE BONE GRAFT FOR UNUNITED FRACTURES

Plating

The great majority of surgeons treat ununited fractures by bone grafting (*see* Figs. 81, 82, 83, 84); a few prefer to treat them by plating after freshening the bone ends. No doubt union can very often be achieved by plating but it is doubtful if the percentage of successes is as high as it is in grafting. None the less, when a deformity is being corrected and there is considerable longitudinal stress it may be well to reinforce the graft by a plate. Other expedients such as mere freshening of the bone ends or making a wedge or step are often unsuccessful and are seldom employed. Drilling of the bone ends, with the object of making channels from one fragment to the other from which new bone can form across the pseudarthrosis, has been extensively employed but the results have not been satisfactory.

As reinforcement



FIG. 81.—Bone grafting for ununited fractures. Stage 1, the biceps is retracted inwards and the brachialis is split longitudinally between its outer two quarters.

(1) Conditions at the fracture site

Treatment by grafting will be influenced by certain conditions which may be found at the site of fracture. Amongst the most important of these are those discussed below.

(*a*) *The condition of the bone ends*

Good apposition

When there is good apposition and alignment and the bone ends are not densely sclerosed it is unnecessary to freshen the bone ends. This is especially so when an inlay graft is used (Burrows, 1940). In cases in which there is displacement it must be reduced as it is important to obtain wide apposition of the bone ends. This will necessitate a wide exposure, excision of scar tissue and freshening and shaping of the bone ends.

Displacement

(*b*) *Loss of bone*

Shortening

Bridging a gap adds slightly to the risk of failure and may be avoided by accepting some shortening. None the less, bridging a gap can nearly always be

successfully achieved by adding to a stout strut of cortical bone pieces of cancellous bone from the ilium. Cancellous bone alone, however effective in reconstructing a jaw (Mowlem, 1944), is sometimes unsuccessful in the long bones. Like war-time food, it gives bulk without strength, and a re-fracture may occur. Further, if it is broken up into small chips, as has been recommended, these chips may not fuse together.

(c) *After infected compound fracture*

When the fracture has been infected, all evidence of infection must have disappeared at least three months before grafting is undertaken. Even then lighting up of infection cannot always be prevented. If a pocket of pus is unexpectedly discovered the operation should be delayed until it is proved that the wound is sterile. Penicillin has greatly diminished this danger, but even so a latent infection by a penicillin-insensitive organism such as *Bacillus proteus* may be lit up. *Sterile bone essential*

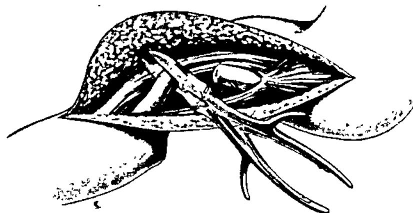


FIG. 82.—Bone grafting for ununited fractures. Stage 2, freshening the bone ends.

(d) *Condition of the skin*

Scar tissue in the operation area, especially when the skin is involved and is adherent to the bone, must be excised before a reconstructive operation on the bone is undertaken. Otherwise sloughing will expose the bone and infection may follow. A full thickness skin graft is necessary. This unfortunately will delay the bone-grafting operation for three months. *Excision of scar tissue*

(e) *Contractures*

Contractures of joints as far as possible should be corrected before bone grafting is undertaken. For instance a patient with an ununited fracture of the tibia which has been badly treated often has talipes equinus. This should be forcibly corrected before the graft is fixed. Otherwise when walking begins the deformity will tend to cause angulation of the graft at the fracture site. *Correction*

(2) Choice of method

As already stated, some form of bone graft is the treatment of choice for ununited fractures. As a rule the graft should be as bulky as the host bone

will take, both for reasons of splintage and for the supply of osteogenic tissue. The onlay graft is, generally speaking, the most suitable; it has the advantage that a massive graft can be applied whereas the inlay graft is limited in mass by the size of the trough which can be made in the receiving bone. Thus the inlay graft is unsuitable for smaller bones like the radius and the ulna but may be used for the femur and the tibia. The onlay graft has the further advantage that it is easier to apply as it requires less skill in joinery.

The onlay graft

There are a few conditions, however, for which the onlay graft is not suitable. For instance in very small bones like phalanges and metacarpals where tendons are closely applied to the bone, the inlay graft is preferable as the

The inlay graft

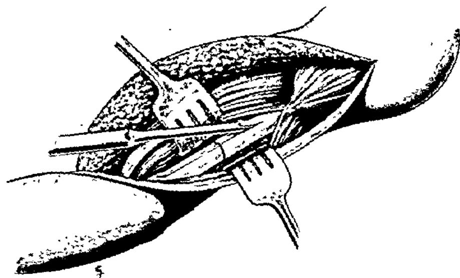


FIG. 83.—Bone grafting for ununited fractures. Stage 3, making a flat surface for the onlay graft.

shape of the bone is unaltered by it. Further, the inlay graft is preferred in cases of non-union with good apposition and alignment, in which it is unnecessary to freshen the bone ends, because the making of the bed necessarily replaces a large part of the fracture line. Finally when the limb is extensively scarred the increased width of the bone which the onlay graft produces may make it difficult to suture the skin without tension.

The sliding inlay graft

The sliding inlay graft is open to the objection that the graft, coming from near the pseudarthrosis, is not in such good condition as one taken from a normal bone. None the less, the method is very successful in the tibia, where a sufficiently stout graft can be obtained; as the tibia is also subcutaneous the necessary additional length of exposure is no disadvantage.

The double onlay graft

The double onlay graft is a formidable procedure and its use may be restricted to cases in which union is particularly difficult to achieve, as in bridging a wide gap.

(3) After-treatment

After operation the most convenient form of splintage is the plaster-of-Paris cast. The cast should be applied over an abundant dressing of cotton-wool and should be divided from top to bottom so that it can be easily opened in the event of undue swelling. *Plaster cast*

At the end of a fortnight when the reactionary swelling has subsided the stitches are removed and a close-fitting cast is applied, immobilizing the joints above and below. This should be retained until there is x-ray evidence of sufficient union, which is obtained usually after a period of from three to five months. *Close-fitting cast*

After the application of the close-fitting cast the maximum activity compatible *Maximum activity*

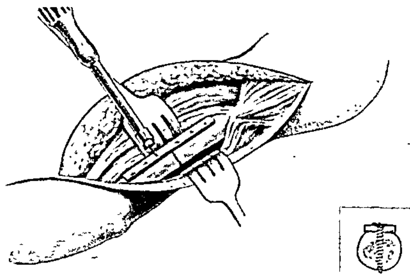


FIG. 84.—Bone grafting for ununited fractures. Stage 4, the onlay graft screwed into position.

with the cast should be encouraged. For instance a patient in whom a graft has been inserted in the forearm should use his hand and shoulder freely; after grafting of the tibia has been done the patient should walk at the third week.

(4) Results, and cause of failure

Published statistics of grafting for ununited fractures show approximately 90 per cent success (Campbell; Speed, 1930; Albee). The principal cause of failure was sepsis. Gross sepsis causes necrosis and sequestration of the graft; mild sepsis by no means makes failure inevitable, for with drainage and continued immobilization the graft may survive. *Sepsis as principal cause*

Sepsis may occur as the result of the lighting up of previous infection in a compound fracture or it may be introduced at operation. Operations on bone are more likely to become infected than are operations on the abdomen as the peritoneum has considerable bactericidal properties. The same is true although to a lesser extent of synovial membrane. Further, however gentle the operator may be, the necessary extensive exposure must entail considerable *Infection at operation*

trauma to the tissues and, consequently, slight contamination, which might be controlled in the abdomen or in a joint, may have damaging effects.

Lately the use of penicillin has greatly diminished the risk of failure from sepsis. Almost equally important now as causes of failure are the persistence of bending strain and insufficient contact with and fixation to the host bone.

(5) Special bones

Henry's approaches

One of the surgeon's chief anxieties in operating on a limb is the danger of injuring a nerve. In this respect Henry's (1927) approaches to the less accessible of the long bones will be of great assistance (*see* Fig. 85). The approaches are planned so that the exposure can be increased to the whole length of bone with the minimal risk of injuring important structures. Access to the bone is gained between the areas of distribution of the main nerves. There is no need therefore as in many other approaches first to identify and isolate a nerve.



Fig. 85.—The skin incision for Henry's approach to the lower half of the humerus.

(a) *Humerus*

Associated injury

The common site for ununited fractures in the humerus is in its lower third. The elbow joint is often stiff, movement taking place at the pseudarthrosis. If in a gunshot wound there is associated injury to the musculospiral or other nerve which requires to be sutured, the nerve suture should be done at the same operation when the bone can be shortened so as to obtain easy approximation of the nerve ends. The massive onlay graft is the most suitable type for the humerus.

Remedying a gap

When there is a large gap involving one or other end of the humerus, as after the removal of a benign giant-celled tumour or other similar condition, the defect may be remedied at the upper end by the use of the required length of the upper part of the fibula with its articular surface; or at the lower end by the use of a suitably shaped graft of tibial cortex.

(b) *Radius and ulna*

Non-union of one or both bones of the forearm without gap or deformity is a relatively simple problem and is suitably dealt with by onlay grafting, but repair after excessive damage, as in a gunshot wound, may be one of the most difficult of surgical procedures.

Excessive damage

It may be impossible to correct deformity from fibrosis and contracture of the muscles without extensive freeing of the bones from their muscular attachments and from the interosseous membrane, and shortening of one bone may not be overcome on account of the difficulty in stretching the muscles and fascia. It will then be necessary to accept the shortening and to shorten the other bone to equalize the length.

Shortening

Simultaneous incisions

In order to avoid cross union when both bones are operated on they should be approached through separate incisions which are open at the same time.

(c) *Scaphoid*

The use of bone grafting in the scaphoid is best restricted to those rare cases of non-union in which the bone ends are sclerosed and in which there is not *Absence or presence of arthritis*

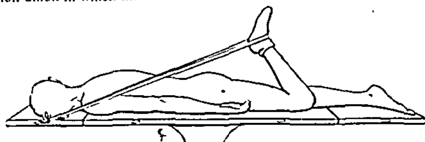


FIG. 86.—Diagram showing position of patient for grafting of the spine. The knee is flexed to give access to the tibia for cutting the graft.

any evidence of arthritis. When arthritis is established the condition is not improved by grafting although the fracture unites. In delayed union, when the x-ray shows a cyst-like widening of the fracture line, grafting is unnecessary, for union will occur with immobilization in plaster.

If grafting must be done, there is a choice of two methods, (1) open or (2) closed. In the former, the dorsal surface of the bone is exposed and a graft is inserted under direct vision. This method has the disadvantage of impairing the blood supply, which enters largely through this aspect. *Open method*

In the closed method (Armstrong, 1941) a peg graft is inserted under x-ray guidance through a small incision over the tubercle. Injury to the blood supply is avoided but the operation is difficult. *Closed method*

(d) *Neck of femur*

A length of the fibula has long been used by Nordenbos for fractures of the neck of the femur but the majority of surgeons use the Smith-Petersen pin for a recent fracture. *Smith-Petersen pin*

For an untreated fracture a graft is often used in addition to a pin but some prefer to perform a high osteotomy and to displace the shaft inwards (McMurray, 1938).



FIG. 87.—Arthrodesis of spine. Rawing the surfaces of the spinous processes with an electric burr.

(e) *Femur*

A massive onlay graft or, perhaps to a lesser degree, an inlay graft is the most suitable for the femur but whichever type is employed a successful

result is imperilled by the strong muscular forces which act on the femur.

Mobility

The danger is increased if after correction of deformity there persists a tendency to angulation. It is therefore especially important to provide effective external fixation. The immobilization given by a plaster spica alone is inadequate. Transfixion pins, piercing the plaster and the limb above and below the operation site, should be added. Skeletal traction with a pin through the lower end of the femur and a pull of about 15 pounds is recommended by some.

External fixation

Plating

As a result of an unsuccessful experience with a few grafts of the femur I have used plating instead of grafting for ununited fractures of this bone. The bone ends are freshened and a long stout plate with 8 screws penetrating both cortices is applied. Of the 8 cases I have treated all were successful. Lately I have been using a Kunscher nail and small grafts placed around the fracture site.

FIG. 88.—Arthrodesis of spine, showing the grafts in place and screwed to the spinous processes.

(f) Tibia

The sliding graft

Some authorities recommend an onlay or inlay graft taken from the opposite tibia. I prefer the sliding graft, having had successful experience of the method (Burns and Michaëlis, 1944). It is rarely necessary to use the less accessible outer surface but when the subcutaneous surface is used it is essential, in the lower half of the tibia, to countersink the lower end of the graft in order to restore the normal varus curve.

Influence of fibula

In the correction of malalignment or when the bone ends have been freshened the intact fibula may keep the tibial bone ends apart. The fibula should then be fractured and the shortening accepted; it will rarely be more than ¾ inch. When there has been gross loss of substance, with a gap left, the latter must be bridged by a sliding graft to which is added cancellous bone from the ilium.

3. THE BONE GRAFT IN ARTHRODESIS

(1) Uses

At some stage in disease or degeneration of a joint the joint ceases to be an asset and becomes a liability. Movement becomes painful and very much restricted and the value of what is left of movement may be far outweighed

by the pain the movement causes. At this stage, with few exceptions, the object in treatment is to provide permanent and complete immobilization of the joint either by external apparatus or, commonly, by arthrodesis.

Indications for arthrodesis

Joints are arthrodesed in the following conditions.

(a) Tuberculous arthritis.
(b) Infective and rheumatoid arthritis.
(c) Osteoarthritis, which includes mechanical arthritis, after trauma.
(d) Paralysis, infantile, spastic or traumatic.
(e) Congenital deformities, such as neglected congenital dislocation of the hip, and club-foot.

Formerly, as Brittain pointed out, arthrodesis was usually attempted merely by removing the articular cartilages, but opposing raw surfaces do not tend to fuse together as readily as do fractured bones and many failures occurred. Nowadays it is the exception to attempt arthrodesis without the use of a graft and much better results are obtained. In many joints the removal of the articular surfaces results in a disparity in size of the opposing bone ends and it is often necessary to borrow bone in order to obtain adequate contact. Further, a graft provides internal fixation.

Arthrodesis plus graft

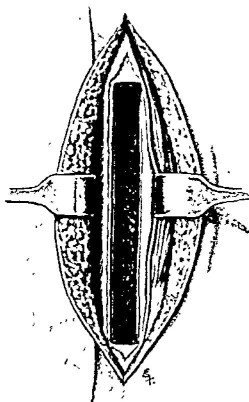


FIG. 89.—Tibia after graft has been removed from subcutaneous surface.

When arthrodesing a joint which is almost ankylosed but is in a good position the difficulty of restoring the alignment after excising the bone ends can be avoided by gouging out a transverse cylinder including the articular cartilage, and filling up the hole either by replacing the removed cancellous bone or by filling it with iliac chips (Pridie).

Extra-articular arthrodesis

Extra-articular arthrodesis depends upon the graft alone. This method is used when it is necessary to avoid a diseased area, as in tuberculous disease of the hip, or for anatomical convenience, as in the Albee fusion of the spine.

(2) Special instances

Some typical instances to illustrate the use of the graft in arthrodesis are given below.

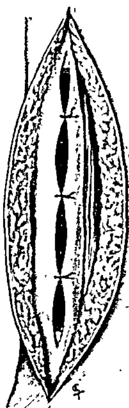


Fig. 90.—After removal of graft from the tibia, the edges of the tibial periosteum are sewn together as closely as possible.

(*a*) *Arthrodesis of spine*

This procedure is sometimes performed:

Pott's disease

(i) In the treatment of Pott's disease. There is no general agreement about its value but it is often performed when the disease has become quiescent after a year or more of recumbency. It is hoped thereby to lessen the chances of recurrence of active disease or of increase of deformity.

Trauma

(ii) In traumatic conditions such as a dislocation in which the reduction is unstable, or a gross compression fracture, in order to prevent deformity or to retain reduction.

Pain

(iii) For certain painful conditions especially of the low back, for instance spondylolisthesis or localized osteoarthritis.

Scoliosis

(iv) For the maintenance of correction of deformity in scoliosis.

Technique

The Albee type of graft is commonly used. This entails the placing of the graft in a bed made by splitting the spinous processes. If a curved graft is required it can be cut in that shape from the tibia or it can be taken from the crest of the ilium.

A modification of this type of graft, giving an increased area of bony contact

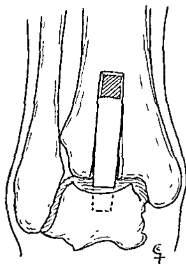


Fig. 91.—Arthrodesis of ankle. Watson-Jones's method.

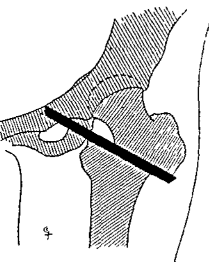


Fig. 92.—Diagram to show ischio-femoral arthrodesis. (*Brittain.*)

and more rigid fixation, is illustrated in Fig. 88. The spinous processes and adjacent parts of the laminae are rawed with a burr, and two grafts, one on each side, are clamped together with screws. The graft should not be longer than is necessary; it is usually enough to include one vertebra above and one below the diseased or injured area. (*See* Figs. 86, 87, 88, 89, 90.)

(*b*) *Arthrodesis of ankle*

The use of a graft makes fusion more certain. After the articular cartilage has been removed from the opposing joint surfaces a graft is slid down from the subcutaneous surface of the tibia and embedded in a slot made in the neck of the astragalus (Watson-Jones, 1943). (Fig. 91.) Bone chips are packed in to occupy the space left by the removal of the articular cartilage. *Technique*

(*c*) *Ischio-femoral arthrodesis*

This is an extra-articular arthrodesis and is eminently suitable for tuberculous hips. It is also very useful in any condition in which the correction of fixed deformity is required in addition to fusion of the joint, such as in osteoarthritis with adduction (Brittain). *Tuberculosis*

An osteotomy of the femur is performed just below the level of the lower surface of the neck. The osteotome is driven inward through the fracture until it penetrates the lower ramus of the ischium. Another osteotome is driven in alongside the first in order to widen the slot enough to take the graft. The graft, which consists of about four inches of the whole of the subcutaneous surface of the tibia, is then driven home until it is firmly embedded in the ischium. (*See* Fig. 92.) *Technique*

4. CONCLUSION

Success in bone grafting depends essentially upon the conditions in which the operation is done. The surgeon should create such surroundings for his work that he has at his disposal a team trained in bone surgery and a comprehensive range of instruments for bone surgery. Above all he should have absolute confidence in the asepsis of his operating theatre and of its staff. *Conclusion*

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[References to other titles are given under Bone Grafting in the Index Volume.]

BONES—ACUTE AND CHRONIC INFECTIONS

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1. INTRODUCTION

66.] The subject chosen for this paper is a large one, and in the space allotted it is not possible to do more than give a bird's-eye view of the field, picking out the salient features.

Principally, acute and chronic pyogenic osteomyelitis will be discussed, and under the heading "Special types" brief mention only will be made of tuberculous osteomyelitis, sclerosing osteomyelitis of Garré, pneumococcal and typhoid infections.

2. SURGICAL ANATOMY

The metaphysis Attention will be drawn merely to the metaphysis, the most important part in relation to bone infection, since it is the area of greatest vascularity, of growth, and of most intense cell activity.

Blood supply Of the 4 sources of blood supply to bone, 3 anastomose in the region of the metaphysis. The nutrient artery, branching up and down the shaft, anastomoses with (1) the metaphyseal arteries, and (2) the epiphyseal vessels, both of which come from the circulus vasculosus of Hunter. The periosteal vessels, running inwards from the periosteum, supply the superficial part of the cortex.

3. AETIOLOGY: ACUTE HAEMATOGENOUS OSTEOMYELITIS

(1) The organisms concerned

The commonest organism is the *Staphylococcus aureus*, and in 400 cases investigated, Fraser (1924) found 78 per cent to be due to this type. His figures are as follows:

The organism

Staphylococcus aureus	78 per cent
Staphylococcus albus	2 per cent
Streptococcus pyogenes	6 per cent
Pneumococcus	14 per cent
Bacillus coli communis	1 case
Bacillus typhosus	3 cases

These figures are similar to those of many other observers, and in any case in patients over 2 years old the chances are 10 to 1 (Key, 1942) that the organism will be *Staph. aureus*. In children under the age of 2 the streptococcus is fairly commonly the causal organism, Green and Shannon (1936) finding it in 63 per cent of 76 cases in young children.

Key puts the figure at 40 to 50 per cent.

(2) The route of infection

Primary foci The infection is commonly blood-borne from some distant focus such as furunculosis, septic tonsils, infected sinuses, blisters and abrasions.

Umbilical sepsis Another source of infection which Fraser believes to be of considerable importance is umbilical sepsis, a mild blood infection occurring at the division of the cord and persisting until the later years of childhood.

Key states that, in his opinion, a patient does not have septicaemia before osteomyelitis develops, but that from time to time there are a few casual pyogenic organisms in the blood stream, probably in all persons, which are usually rendered harmless by natural processes, and are of no clinical importance unless they become held up in the bone, and there multiply.

(3) The localizing factors

(a) Anatomical and physiological factors

Anatomically, the metaphyses of long bones may be said to consist of wide, blood-filled spaces, lined by endothelium and crossed by delicate bone lamellae. *Structure of the metaphysis*

The blood flow, coming from the narrow vessels into these open spaces, and also meeting the resistance of the crossing lamellae, will naturally slow down appreciably, giving blood cells and organisms the chance to lodge on the walls of this semi-stagnant backwater. *Stagnant blood flow*

Another factor, theoretically of importance, was demonstrated by Hobo (1921). He injected organisms into the blood stream, finding them evenly distributed throughout the medulla at the end of 3 hours, but after a further 4 to 6 hours the diaphysis was clear, organisms being found in the metaphysis only. Hobo interpreted this as an indication that phagocytosis, active in the shaft, was deficient in the metaphysis.

(b) Incidental factors

Among these, trauma stands out as being of supreme importance. The trauma may be considerable, or the merest sprain; enough, however, to spring a few delicate lamellae and cause a small intrametaphyseal haemorrhage and a greater liability to deposition of organisms.

The disease occurs six times more often in boys than in girls, most frequently between the tenth and fifteenth years, and it is reasonable to assume that a male child is more liable to trauma, from the very nature of his games.

The sites most commonly affected are the upper metaphysis of the tibia and the lower metaphysis of the femur. The large size of these metaphyses carries an obvious liability to trauma. *The exposed metaphysis most commonly affected*

4. PATHOLOGY

(1) Acute osteomyelitis

The pathological process begins as a small area of intense inflammatory reaction in the metaphysis. As bacteria multiply exotoxins are liberated, causing death of cells in the vicinity, and suppuration ensues. The pus gathers under tension, and tension, combined with infection, leads to early thrombosis of vessels. *Formation of pus*

The pus spreads outwards through the cancellous bone to the cortex, along the line of the epiphysis (Starr, 1922): traversing the Haversian and Volkmann canals, it reaches the subperiosteal area whence it spreads downwards raising the periosteum from the bone (*see* Fig. 93). *Spread of infection*

Absorption, brought about by osteoclasts and cells of the inflammatory tissues, begins soon after the primary focus of acute inflammation, and results in the areas of rarefaction seen in x-ray pictures as the first radiological evidence of disease. It is absorption of the delicate lamellae of the growing area, and is of living, not dead, bone. *Absorption of bone*

Necrosis and sequestration

Bacteria and their toxins, plus the important factor of diminished blood supply, are responsible for necrosis, which may be quite small in extent, or include the whole diaphysis if completely surrounded by pus. Absorption of a certain amount of necrotic cancellous bone occurs, but pieces of any considerable size, and necrotic compact bone, usually form sequestra. (*See* Fig. 94.)



Fig. 93.—Acute osteomyelitis: early phase showing the raising of the periosteum.

Formation of new bone

Whilst the above changes are taking place, natural forces begin to reassert themselves. New bone is formed under the raised periosteum (*see* Fig. 95); vascular granulation tissue forms between the living and dead bone, separating the latter off as a sequestrum (Fig. 95); endosteal new bone results in thickening and increase in density of the shaft.

(2) Chronic osteomyelitis

(*a*) *Chronic osteomyelitis following acute osteomyelitis*

In the vast majority of cases a legacy of the acute disease, the principal pathological features of the chronic phase are the presence of unabsorbed sequestra and unobliterated cavities, containing infected granulation tissue, pus and sometimes necrotic bone.

Natural healing unlikely

Natural processes are unable to obliterate the cavity, the rigidity of its walls preventing collapse, and it becomes gradually surrounded by dense sclerotic bone. A sinus may lead to the exterior, which continuously or intermittently discharges pus. Sequestra may be discharged to the surface via this route, and healing occur, but they are usually retained, merely serving to keep up infection. Discharge continued over many years may in rare cases give rise to epithelioma (Benedict, 1931).

Complications

Chronic osteomyelitis is subject to an occasional acute flare-up, which may occur some years after the condition has apparently healed. Another complication is metastatic osteomyelitis, an acute focus appearing in some distant site, possibly at some distant date.

(*b*) *Chronic osteomyelitis arising insidiously*

Brodie's abscess

This is comparatively rare. Due to organisms of attenuated virulence, usually *Staph. aureus*, an inflammation of low grade sets in, causing limited bone destruction and soon becoming surrounded by a proliferative defensive reaction. A small abscess results, surrounded by an area of dense sclerosis

(Brodie's abscess), commonly situated at one or other end of the tibia. (*See* Fig. 96.)

Pain of a dull, boring nature, usually worse at night, is the most prominent symptom. It may be felt on and off for some considerable time. Occasionally



FIG. 94.—Acute osteomyelitis: an extremely acute case. Absorption is widespread, causing a pathological fracture of the neck of the femur. A large sequestrum is well shown just below the head.

there may be a slight rise in temperature, with some reddening of the overlying skin, and mild constitutional disturbances. The diagnosis is established by x-ray examination.

(c) *Special types*

(i) *Pneumococcal osteomyelitis.*—This condition differs from the staphylococcal variety in some important respects, running a fairly mild course, causing few constitutional symptoms and less marked local manifestations. *A less severe disease than the staphylococcal infection*

Pathologically, pus formation is slight, and may even be absent, a serous effusion occurring. Bone destruction and new bone formation are much less evident.

Complete resolution and healing is likely to occur under conservative treatment.



FIG. 95.—Acute osteomyelitis: an involucrum has formed round the shaft of the ulna. On the dorsal side a long sequestrum is being separated.

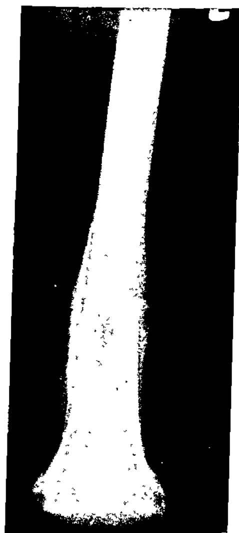


FIG. 96.—Brodie's abscess, lower end of femur. The cavity has been present for some years and has moved away from the end of the bone as growth has proceeded. (*By courtesy of Mr. Walter Mercer.*)

(ii) *Typhoid osteomyelitis.*—Six to eight weeks after the onset of typhoid fever, a patient may complain of pain in one of the bones, commonly the ribs, tibia, ulna, sternum or pelvis. The infection reaches the bone during the septicaemic stage of the disease. Occasionally there is a latent period, perhaps of several years, before bone infection becomes manifest.

Usually of a subacute type, bone changes are not marked, and abscess formation uncommon. The infection may result only in some bone sclerosis.

If an abscess forms it should be drained, a few holes being drilled in the bone, the wound packed and the limb incorporated in plaster. In most cases healing will have occurred in a few months, and there should be no further trouble.

Drain abscesses

If sclerosis is present, where possible, as in a rib, the whole area should be excised and primary suture performed.

(iii) *Sclerosing osteomyelitis of Garré.*—This is a rare condition affecting principally the shafts of long bones. It may be ushered in by an acute attack with pain and swelling over the affected site. Pus formation does not occur, and the acute phase gradually subsides leaving the bone considerably thickened. There is a gradually increasing sclerosis which may proceed to complete obliteration of the medullary canal. The disease is subject to an occasional flare up, each of which results in the formation of yet more bone.

Key recommends opening the bone and excising a segment of sclerotic bone down to the medulla. If a cavity is encountered saucerization is performed and the wound closed, with a small drain down to bone. After this procedure the condition will settle down, but of course the thickening of the bone remains.

(iv) *Tuberculous osteomyelitis.*—Commonly infecting children in the first decade of life, the bones most frequently involved are those of the hands and feet (dactylitis), the tibia, ulna, vertebrae and skull bones (from tuberculous mastoiditis). The disease is a secondary blood-borne infection.

Once the infection is established, the usual tuberculous changes follow, leading to marked decalcification. New bone formation is scanty.

Granulation tissue forms and caseation follows

Grossly, there are two principal forms, (1) infiltrative, seen typically in metacarpals and phalanges, and (2) encysted, seen in the metaphyses of long bones.

In the encysted type, McMurray (1943) recommends opening up the infected area, clearing out all infected tissue very thoroughly, and closing the wound without drainage.

Primary suture

For the spreading type of disease, conservative measures are recommended, fixing the part in plaster. If conservatism fails to check the infiltration, operation may be called for, the procedure of diaphysectomy being carried out. In a severe spreading tuberculous condition the possibility of non-union or failure of regeneration is considered a justifiable risk.

5. CLINICAL PICTURE: ACUTE HAEMATOGENOUS OSTEOMYELITIS

In a typical case, acute haematogenous osteomyelitis begins quite suddenly, being ushered in by a rigor, high temperature and intense throbbing pain in the bone; sometimes pain is the first manifestation. All the features of a severe general infection are present, and in the later stages, with increasing toxaemia, delirium may supervene.

On inspecting the limb, it will be found to be held motionless, with the related joint in flexion. Tenderness is the earliest local sign, extreme over the site of the primary focus. Redness of the overlying skin follows, with local temperature increase, and later oedema, which is a fairly accurate indication of underlying pus.

Local appearances

Pathologically, pus formation is slight, and may even be absent, a serous effusion occurring. Bone destruction and new bone formation are much less evident.

Complete resolution and healing is likely to occur under conservative treatment.



FIG. 95.—Acute osteomyelitis: an involucrum has formed round the shaft of the ulna. On the dorsal side a long sequestrum is being separated.

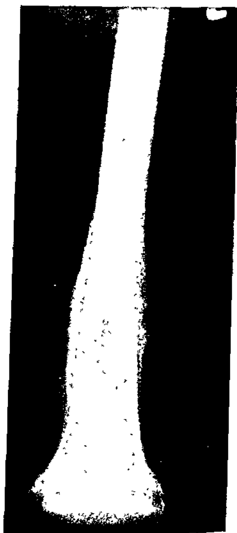


FIG. 96.—Brodie's abscess, lower end of femur. The cavity has been present for some years and has moved away from the end of the bone as growth has proceeded. (*By courtesy of Mr. Walter Mercer.*)

(ii) *Typhoid osteomyelitis.*—Six to eight weeks after the onset of typhoid fever, a patient may complain of pain in one of the bones, commonly the ribs, tibia, ulna, sternum or pelvis. The infection reaches the bone during the septicaemic stage of the disease. Occasionally there is a latent period, perhaps of several years, before bone infection becomes manifest.

Usually of a subacute type, bone changes are not marked, and abscess formation uncommon. The infection may result only in some bone sclerosis.

resemblance between the two. Severe pain, in the vicinity of a single joint, of sudden onset, occurring in a child previously healthy bears no resemblance to acute rheumatic fever. The toxaemic manifestations in osteomyelitis are very much more marked, as is the local pain and tenderness.

In a comparatively mild case of osteomyelitis the error is less serious, but it should not occur. Acute rheumatic fever is a polyarticular disease.

8. PROGNOSIS

It is not possible to give exact mortality figures for acute osteomyelitis. Figures varying in the extreme have been given from time to time in the literature, which obviously must reflect the severity of the disease in the particular series of cases being reported. During the course of any individual case, however, there are certain factors to be taken into consideration, upon which one can base a prognosis. These can be enumerated as follows.

(1) Age

In acute osteomyelitis, unlike most other conditions, the disease is usually less severe and less dangerous to life in the first three years than in later childhood (Fraser, 1936). There are two principal conditions responsible for this; first, up to the age of two, 40 to 50 per cent of cases are due to a streptococcus, and secondly, the bone in so young a person is much more porous than in later years, and as the pus makes its way to the surface more easily there is less liability to septic absorption. *Better prognosis in younger patients*

(2) The organism concerned

Infection by the *Staph. aureus* is the most serious, both in regard to immediate mortality and future crippling.

(3) The site affected

The nearer to the trunk the worse the prognosis. An infection in the upper metaphysis of the femur is more serious than one of equal degree in the upper end of the tibia. A metaphysis partly or wholly lying within the synovial reflection affects the prognosis adversely, as concurrent joint infection can so easily occur. *Danger of joint infection*

(4) Systemic manifestations

The more marked the systemic manifestations, the more grave is the outlook. A temperature rising up to 104° F. or even higher, an excessively rapid pulse of poor volume, a gradually diminishing urinary output, and snatches of delirium, are all harbingers of a fatal ending. *The general condition as an index*

(5) Laboratory findings

Adverse findings are two or more positive blood cultures, an unduly low leucocyte count, and a rapidly falling erythrocyte count, indicating infection with a haemolytic strain of staphylococcus.

(6) Local prognosis

A chronic osteomyelitis is likely to develop in the vast majority of cases, and of these chronic cases, it must be remembered that some, in spite of every endeavour, will never clear up, and the limb may have to be sacrificed to preserve the general health of the individual. *Long-continued suppuration may lead to amyloidosis*

Apparent improvement

A temporary improvement in the general symptoms may occur coincidental with the escape of pus into the subperiosteal region, and with consequent easing of the tension within the bone.

6. SPECIAL AIDS TO DIAGNOSIS

There are no special diagnostic tests of cardinal value in a case of acute osteomyelitis, but blood culture and a blood count are useful adjuncts to clinical acumen.

Leucocytosis present

The blood count will usually show a leucocytosis, in a severe case, up to 20,000, the majority of cells being neutrophils. The erythrocyte count, in a very toxic case, may fall appreciably, and the degree of anaemia eventually may be very marked. A positive blood culture is helpful, both as a confirmatory factor in diagnosis, and also from the point of view of treatment.

X-rays as a diagnostic aid are of little help, as there is seldom any radiological evidence during the first 10 to 14 days, although I have seen rarefaction as early as the sixth day.

7. DIFFERENTIAL DIAGNOSIS

There are certain conditions with which it is possible to confuse acute osteomyelitis, and these must be borne in mind when making the diagnosis.

(1) Cellulitis

Cellulitis affecting the soft tissue overlying a bone, especially when overlying the metaphysis, bears a superficial resemblance. The area of redness, however, is more widespread, the pain and toxaemia are less than in osteomyelitis, and the tenderness is less marked and more diffuse.

(2) Erysipelas

Similar conditions to cellulitis prevail here. In addition, the well-defined raised edge, plus the small vesicles near the spreading margin, should make the diagnosis clear. The lymph glands draining the area are usually enlarged and tender.

(3) Pyogenic arthritis

In this condition joint symptoms predominate and confusion should not arise. Muscle spasm is intense; the slightest movement causes extreme pain, and the joint swelling is much more marked than would be accounted for by the reactionary synovial effusion seen in osteomyelitis.

(4) Infantile scurvy

Scurvy may prove difficult to differentiate

Intrametaphyseal and subperiosteal haemorrhage, giving rise to pain and tenderness, create a superficial resemblance to acute osteomyelitis. The intense pain and severe general symptoms are, however, absent. A history suggestive of extremely poor feeding, previous subcutaneous haemorrhages, haematuria and the finding of congested, spongy gums, should make the diagnosis clear.

(5) Acute rheumatic fever

Acute rheumatism is seldom, if ever, mistaken for acute osteomyelitis, and yet the reverse mistake frequently occurs. It should not occur as there is little

formed. A patient so treated must be watched carefully, as very rapid change can occur, and any marked rise in pulse rate, increase of pain and worsening of systemic manifestations, must be interpreted as indicating a failure of balance between the septic process and natural defences. Active treatment should be instituted at once and operation performed.

(iv) When a patient is seen with signs of profound toxaemia, and in a poor general condition, operation should be delayed for a few hours, until such time as the patient is fit to stand an anaesthetic and a minimal degree of interference with the bone. In such a case energetic pre-operative measures are instituted at once. *Unfit to stand operation*

(c) *Conservative treatment*

The essentials of conservative treatment may be summarized as follows.

(i) *Immobilization of the limb.*—This is best obtained by a light, well-padded plaster, extending to include the joint above and below the site affected.

(ii) *Relief of pain.*—Rest must be assured at all costs by suitable sedatives. Morphine is usually necessary.

(iii) *Administration of fluid.*—Large quantities of fluid must be given, and although the patient may be perfectly capable of drinking, most individuals will take only enough to satisfy thirst, in spite of exhortation. For these reasons, I believe it is more satisfactory, in the vast majority of cases, to set up an intravenous drip of glucose-saline.

(iv) *Chemotherapy.*—Sulphathiazole or sulphadiazine must be given in full doses, by mouth or intravenously. We have found Cibazol through the drip most satisfactory.

(v) *Blood transfusion.*—In a severe case with haemolysis occurring, the administration of a blood drip may prove of very great benefit.

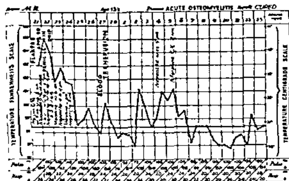


Fig. 97.

(2) **Penicillin available**

Under these circumstances the treatment should be definitely conservative, even in the most severe cases, provided the disease is seen at an early stage. Surgery may still be required for later cases, with a subperiosteal, or even a soft-tissue abscess, but such remarkable results have already been achieved with penicillin and conservative treatment, that this is likely to become the method of choice for early cases.

The temperature chart illustrated in Fig. 97 is that of a girl aged 13½ years, who was admitted to Edinburgh Royal Infirmary with an overwhelming toxaemia and an extremely acute local lesion. The patient was completely beyond herself, periodically screaming out in agony. Her whole appearance was one of extreme toxaemia and dehydration. The temperature rose up to 105° F. and the pulse rate was 150. The temptation to drill the bone in order *A severe case treated with penicillin*

9. INDICATIONS FOR SURGICAL INTERVENTION

Studying the literature published during the past few years, one is struck by the divergence of opinion regarding treatment by conservatism or early operation. Arguments advanced in favour of both views may be briefly summarized as follows.

(i) *Conservative outlook.*—In favour of conservatism it is argued that the bone lesion is a local manifestation of a generalized septicaemia, and as such may be regarded as a fixation-abscess, which, if left alone will stimulate antibody formation, thus exerting a beneficial effect on the disease. It is also claimed that operation in the earliest stages may encourage, by opening up the soft tissues and bone, a spreading of the infective process and a greater degree of destruction. Operation should be delayed until suppuration is well advanced or even until a subperiosteal abscess has formed, and then should be limited to simple incision and drainage.

Early operation may spread the disease

(ii) *Immediate operation.*—Advocates of immediate operation claim that by this means destruction of bone is reduced and tension is relieved, thereby diminishing septic absorption and lessening the chances of further inoculation of the blood stream.

Early operation prevents disease

The discovery of penicillin has so revolutionized the treatment of acute pyogenic infections that I believe the presence or absence of it to be the most important single factor in deciding between conservative or operative treatment. The problem may be conveniently discussed under two major headings as follows.

Penicillin alters the whole concept of treatment

(1) Penicillin not available

Every case of acute osteomyelitis is an individual problem, and rigid adherence to the principles of conservatism or immediate operation is to be deprecated; discrimination should be practised and the following broad indications may prove helpful.

Treat every case on its merits

(*a*) *Indications for operation*

(i) The presence of pus in the subperiosteal area.

(ii) Suppuration in the soft tissues.

(iii) When the metaphysis affected is partly or wholly intracapsular, operation should be performed as early as possible in an attempt to prevent subperiosteal spread, and consequent infection of the joint.

Danger of joint infection

(iv) Any patient with a moderate to severe infection, provided the general condition is good, is a candidate for early operation, which tends to limit the destruction of bone and to prevent further absorption.

(*b*) *Indications for conservatism*

Conservative treatment may be adopted in the following circumstances.

(i) In infants and young children in the first few years of life, delay should be practised. A large number of these cases are due to the streptococcus; bone destruction and pus formation are much less marked, and pus, if present, gets to the surface comparatively easily.

In the earliest years

(ii) When the infecting organism is known to be one which forms pus in very small amounts, if at all, such as the pneumococcus.

(iii) When the disease, although staphylococcal, is of a very mild nature, operation should be delayed unless, or until, a subperiosteal abscess has

A very mild infection

formed. A patient so treated must be watched carefully, as very rapid change can occur, and any marked rise in pulse rate, increase of pain and worsening of systemic manifestations, must be interpreted as indicating a failure of balance between the septic process and natural defences. Active treatment should be instituted at once and operation performed.

(iv) When a patient is seen with signs of profound toxaemia, and in a poor general condition, operation should be delayed for a few hours, until such time as the patient is fit to stand an anaesthetic and a minimal degree of interference with the bone. In such a case energetic pre-operative measures are instituted at once. *Unfit to stand operation*

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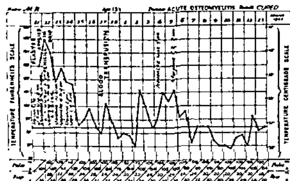


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to obtain relief for the patient was almost irresistible, but a penicillin drip was started and operation withheld.

On the fifth day after starting the penicillin the temperature was normal, and the child's condition was improved tremendously. The temperature rose again on four or five occasions, never higher than 101° F., and after the twentieth day it remained normal.

Fig. 98 is a 4-hourly chart of the first 7 days, and illustrates very well the steady drop in temperature and pulse, which was in step with the gradual improvement in the general condition. Fig. 99 shows the condition of the leg 2½ months after admission.

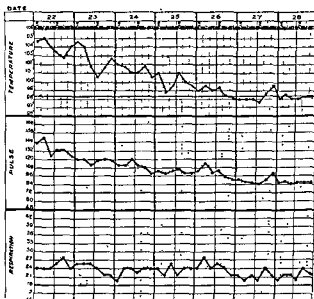


FIG. 98.

Administration

Penicillin is administered by intramuscular drip in most cases—in this particular case the severity of the disease warranted intramuscular and intravenous administration. The amount given is 100,000 units per 24 hours, and usually a total of 1½ million units is administered (15 days). In many cases it will be found to be of great benefit to give penicillin also directly into the medulla at the site of the infection. A strong wide-bore needle is driven through the cortex—quite easily done by hand using a screwing motion; plaster is applied with the needle protruding through the cast, the needle then being connected up with the penicillin drip. In addition the usual conservative measures are adopted, but of course the use of sulphathiazole is not necessary.

10. PRE-OPERATIVE MANAGEMENT

Most of the steps enumerated under conservative treatment are applicable here, except that a protective dressing and splint only are required whilst awaiting operation, plaster, of course, being applied afterwards.

11. OPERATIVE TECHNIQUE

(1) Acute osteomyelitis

Drainage of the bone

The object of operation is to secure drainage of the bone, and this is attained by either metaphyseal drilling or by removal of overlying cortical bone—the "gutter" method.

Metaphyseal drilling causes less trauma and is the treatment of choice in the early case. When it is suspected that spread has reached the medulla it is probably wiser to make a small gutter as it is questionable whether drilling will obtain sufficient drainage.

The preliminary steps in both cases are the same. The limb is placed upon a sand-bag in the most suitable position for exposure of the bone. The incision is placed over the most superficial part of the bone whenever possible, so that soft-tissue disturbance is minimal; it must be of adequate length.

When the soft tissues have been retracted and the bone exposed, the periosteum is incised, taking care to begin the incision away from the epiphyseal line—do not approach nearer than ½ to ¾ an inch. Pus if encountered is evacuated, and if not the periosteum is stripped well back round the bone in case pus lies out of view.

Watch the epiphyseal line



Fig. 99.—Acute osteomyelitis treated with penicillin: Note some areas of rarefaction and slight subperiosteal bone formation only. There is no sequestration and no gross bone destruction. Changes are minimal, yet this was a disease of great severity.

(*a*) *Metaphyseal drilling*

Holes are now drilled in the cortex, beginning near the epiphyseal line and working towards the limits of suppuration. Drilling stops when no further pus is encountered. It is safer to drill almost at right angles to the bone, rather than in the direction of the epiphyseal plate, lest it be damaged. The size of the drill used should be ¼ inch in adults, ⅛ inch in children. Fig. 100 illustrates the principles of the technique.

(*b*) *The gutter method*

When a drill has disclosed pus in the medulla a piece of cortex overlying the metaphysis is removed with a burr, and the resultant opening is enlarged towards the shaft with a small gouge. It is sometimes easier to make three or four burr holes and join them up. The size of the opening made in the cortex varies, but on an average 2 to 3 inches in length and ½ inch in width should suffice (Fig. 101).

After either of these procedures, bleeding points having been ligated, the wound is liberally dusted with sulphathiazole powder, and loosely packed with sterile Vaseline gauze or gauze soaked in acriflavine emulsion. The pack must not be inserted as a tight "plug", or drainage will be prevented. Dressings are applied and the part enclosed in plaster.

Packing must be loose

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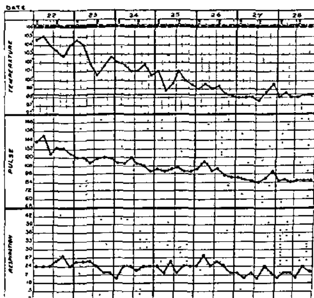


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up, and the walls gently curetted. Saucerization is then proceeded with, more cortical bone being removed if necessary, until the walls slope gently to the centre (Fig. 102).

The tourniquet is now removed, all bleeding points are ligated, and the resultant cavity and wound generously sprinkled with sulphathiazole powder. The cavity is now loosely packed with acriflavine-emulsion gauze, and the extremities of the incision sutured. Dressings are applied followed by a lightly padded plaster cast.

(*b*) *Cavity grafting*

Owing to the situation of the cavity, saucerization may not be feasible, and in that event some form of cavity grafting may be attempted. Various methods have been described, the results, in the main, being disappointing. A muscle graft, however, holds out some prospect of success, as it can be obtained with a good blood supply.

Preparation of cavity for graft

The operation is performed in two stages. As a first stage the cavity is prepared for the graft, overlying cortical bone being removed, any loose pieces of bone taken away and the cavity scraped clean, including the lining membrane. It is then swabbed out with strong tincture of iodine, followed by surgical spirit, and packed with sulphanilamide tulle. Sterile dressings are applied.

Complete asepsis for dressings

Sometime during the next 3 or 4 weeks a full course of sulphathiazole is administered. The packing is changed at intervals under completely aseptic conditions.

The second stage is then completed. A generous incision is made, curved as requisite to overlie nearby muscle and expose the cavity. A flap of muscle of suitable size is freed, swung as little as possible on its blood supply, and turned into the freshened cavity, being sutured to the edge with a few interrupted catgut stitches (Fig. 103).

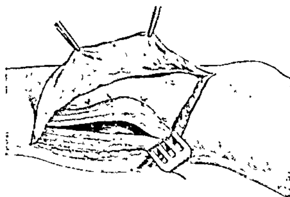


FIG. 103.—Cavity grafting: part of gastrocnemius has been separated in the line of its fibres and swung into the already prepared cavity. Sometimes it is necessary to divide the muscle. Although not so satisfactory, it can be done low down as the vascular bundle enters at the upper end.

Covering the muscle graft with healthy skin is a difficulty, and it is usually necessary to employ skin grafts. Mercer (1936) recommends having a convenient graft prepared beforehand, such as a pedicle graft on the opposite leg.

Reference has already been made to the frequent disappointment attendant upon this method of treatment, the chief causes of failure being persistent infection and the impossibility of bringing healthy skin together in the final stage. With penicillin to control infection, and with grafts to replace scarred

(2) Chronic osteomyelitis

The problems in this condition are retained sequestra and unobliterated bone cavities.

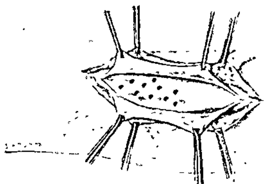


FIG. 100.—Metaphyseal drilling: showing the periosteum reflected and a number of holes drilled in the metaphysis.

Small superficial sequestra may be easily removed

If the sequestrum is small, fairly superficial, and the involucrum overlying not hard and sclerosed, it may be removed by a suitable incision, the overlying involucrum being collapsed by pressure, in an attempt to obliterate any cavity which may be left. The wound is then packed with flavine emulsion, and the prospects of cure are fairly good.

With a larger sequestrum, or one lying in a cavity with rigid sclerosed walls, sequestrectomy combined with saucerization of the cavity is the treatment of choice.

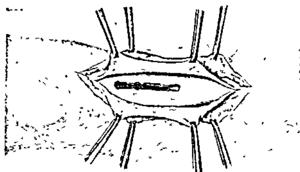


FIG. 101.—The gutter operation. It is better to make the gutter a little short, rather than excise bone overlying healthy medulla. No curettage must be performed—the medulla must be left undisturbed.

(*a*) *Technique*

Tourniquet helpful, but not necessary

A tourniquet is applied and the bone exposed by the most suitable incision, which should be made fairly long as adequate exposure is essential. After retraction of the soft parts, the periosteum is incised and stripped off the affected area with an elevator. Cloacae may be seen at this stage, leading into the cavity. The overlying cortex is then removed, which may prove difficult, owing to the dense sclerosed nature of the bone. One of the simplest ways of accomplishing this stage is to make multiple drill holes, very close to one another, outlining an oval area of bone; a few smart blows with a sharp osteotome should then loosen the fragment outlined, which can be lifted away.

Difficulty of removing cortex

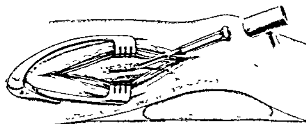


FIG. 102.—Saucerization nearly complete. An overhanging edge is being removed with a gouge.

Any sequestra lying inside the cavity are then removed, or if too large, removed after breaking

After saucerization or sequestrectomy, similar treatment is adopted, but it may be possible to leave the plaster unchanged for a longer period in the first instance.

13. RESULTS OF TREATMENT

In a certain number of cases of the acute disease, provided drainage has been both adequate and early, healing will occur gradually, the discharge becoming less, and the wound filling with healthy granulation tissue. New bone will form and plaster may finally be discarded.

In the majority of cases, however, the condition will pass into the chronic phase, with the formation of one or more sequestra and a discharging sinus.

Saucerization and sequestrectomy, if adequately performed, should lead to healing. The discharge becomes gradually less, and the wound slowly closes in. If the soft tissues are able to fall in and obliterate the cavity, healing is considerably accelerated.

Occasionally, in spite of all efforts, treatment is unsuccessful and, if the continued suppuration is menacing the health of the individual, amputation will be required.

I wish to thank Sir John Fraser, Bt., for his very helpful suggestions and most valuable criticism during the writing of this paper. Figures 100 and 101 are from his collection.

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[References to other titles are given under Bones: Acute and Chronic Infections in the Index Volume. The subject of Bone Diseases is also dealt with in the *British Encyclopaedia of Medical Practice* (1936), Vol. 2, p. 553.]

and damaged skin and soft tissue, a new approach can now be made to tl problem of chronic osteomyelitis. Two conditions are essential for success first, the infected area must be accessible to surgical approach, and secondl the site and extent of the disease must be such as to make complete excisic possible (Robertson and Barron (1946)).

(3) Operation stages

Operation is performed in three stages.

(a) Stage 1

Penicillin is administered by the intramuscular route—either 100,000 uni daily by continuous drip, or 15,000 units every 3 hours—for 24 hou before, and 4 days after, operation. Extensive excision of all diseased tissu including skin, scar tissue and infected bone is carried out, bone resectio being continued till vascular bone is exposed everywhere. Care must be take to preserve the blood supply to the remaining skin, muscles and periosteum The whole wound surface, bone and soft tissue, is then completely covere with grafts of split skin, which "takes" readily on the bone surface and act as a dressing, limits the production of scar tissue, and assists materially in th control of infection. The split-skin graft is applied on tulle gras over whicl cotton-wool pledgets soaked in warm saline solution are packed so that th graft is pressed down evenly over the whole wound surface. A pressure dressin and crêpe bandage are then applied.

(b) Stage 2

It is usual to allow an interval of at least 4 weeks between the healing of stage 1 and the commencement of stage 2. Plastic repair of the soft tissue is then carried out by some form of flap which will provide a good thickness of supple healthy cover to the bone defect. The duration of this stage must depend upon the variety of flap used. In after-treatment it is important that splinting should be light so as not to interfere with the all-important physiotherapy.

(c) Stage 3

Six to eight weeks after the completion of stage 2 the defect in the bone is repaired by bone transplants. When bridging of a gap is necessary autogenous onlay graft is used, and the defect is further filled in with cancellous bone. Whenever possible, the stage of soft-tissue repair should be successfully completed before bone grafting is attempted. In filling a deep cavity, however, the second and third stages may have to be combined, since only after the cavity has been filled can a full-thickness skin cover be obtained. In such circumstances cancellous chips either alone or combined with a muscle graft advancement will be required.

12. POST-OPERATIVE CARE

In the acute case, the plaster applied at operation is changed after the first 2 weeks. The pack is removed, the surrounding skin well cleansed and, after powdering with sulphathiazole, the wound repacked loosely with flavine emulsion or Vaseline gauze. A fresh plaster is then applied. Thereafter it is necessary to apply a fresh plaster and perform repacking approximately every 5 or 6 weeks, depending upon the amount and odour of the discharge.

1. GENERAL

67.] Under the heading of "Bones—Errors of development and growth" are included a number of congenital bony abnormalities, some of which show a strong heredo-familial incidence (having been described in three or more successive generations), and which can be assumed to be transmitted as Mendelian dominants. In others, there is presumptive evidence of recessive inheritance, but often the family histories (particularly with regard to consanguinity, or otherwise, of parents) are too incomplete for a positive statement to be made. In others again the condition appears to arise *de novo*.

These abnormalities may be localized, affecting a single bone, or generalized, affecting part, or the whole, of the skeletal system and sometimes associated with congenital abnormalities of other tissues, such as osteogenesis imperfecta and blue sclerotics, arachnodactylia and ectopia lentis. In the case of localized bone dystrophies, the bone may show partial or complete absence (aplasia), deformity or local gigantism (dysplasia), fusion with adjacent bones (for example fusion of radius and ulna, fusion of vertebrae, syndactyly), or reduplication (for example cervical rib, polydactyly). These lesions may be bilateral or asymmetric. *Localized Generalized*

2. GENERALIZED DYSTROPHIES

Whilst many atypical, and at present unclassifiable, cases occur, it is possible to differentiate a number of more or less well-defined osseous dystrophies. Some of these show a general uniformity both in clinical manifestations and transmission, whereas others show familial variants, intermediary types, and an apparently erratic occurrence, requiring further elucidation.

3. ACHONDROPLASIA

(Chondrodystrophia foetalis; micromelia)

(1) Definition

A disturbance of endochondral bone-growth occurring during foetal life and resulting in shortening of the extremities and dwarfism. The disease has been known since prehistoric times, though the earlier medical writers confused it with foetal rickets, a condition to which it bears no relation. It was clearly distinguished by Parrot in 1879.

(2) Aetiology

The condition affects both sexes and is hereditary (having been traced through six generations in the male line) and frequently familial. It is transmitted as an incomplete Mendelian dominant (Cockayne, 1933). Jansen (1912) suggested amniotic pressure as a causative factor, but it must be considered that apart from the hereditary factor the aetiology is unknown; no hormonal disturbance has been demonstrated.

(3) Surgical anatomy and pathology

Whilst periosteal bone-growth proceeds normally in these cases, there is a severe disturbance of cartilage bone-growth, affecting principally the length of the long bones and the development of the cartilage bones of the cranial axis and the nasal septum; the vertebral column is affected to a variable but usually slighter extent. This unequal growth results in gross shortening of

BONES—ERRORS OF DEVELOPMENT AND GROWTH

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diagnosis is afforded by radiological examination, which shows the grossly shortened long-bones, expanded at the extremities (*see* Fig. 104). The femur is more affected than the bones of the lower leg, and the tibia is often curved and as long as the fibula. The space between metaphysis and epiphysis is reduced.

Whilst there should be no difficulty in the diagnosis of the typical achondroplasiac, particularly when the condition is transmitted as a Mendelian dominant, atypical cases occur suggesting a possible relationship to other types of chondrodysplasia (Parsons, 1936).

(7) Associated syndromes

(*a*) *Punctate epiphyseal dysplasia*

In this condition the long bones show the characteristic deformity of achondroplasia, but there is in addition radiological stippling of the epiphyses and bilateral congenital cataract. Harris (1933), who examined a case histologically, found mucoid degeneration of the cartilaginous vertebrae and ends of the long bones, and considered the fundamental disturbance identical with that in achondroplasia (*see* Fig. 105).



Fig. 105.—Punctate epiphyseal dysplasia. The skiagram shows changes similar to those of achondroplasia, with stippling of epiphyses in addition. The patient also had bilateral congenital cataract.

(*b*) *Chondro-ectodermal dysplasia* (*Ellis–Van Creveld syndrome*)

The association of achondroplasia, ectodermal dysplasia (affecting the hair, teeth and nails), polydactyly and congenital morbus cordis has been described. In 2 out of 3 cases the parents were cousins, suggesting a possible Mendelian recessive factor.

4. ARACHNODACTYLIA

(Acromacria; dolichostenomelia; spider fingers and toes)

(1) Definition

A syndrome consisting of extreme length and slenderness of fingers and toes, and to a lesser extent of arms and legs, associated with congenital dislocation of the lenses in approximately 50 per cent of cases, and with congenital morbus cordis in approximately 30 per cent. The condition was originally described by Marfan in 1896. *Associated malformations*

the limbs, and a characteristic facies due to depression of the nasal bridge whilst the cranial vault and membrane bones of the face have developed normally. Harris (1933) has described the pattern of the femur as consisting of a series of lines of arrested growth in its whole extent, simulating a normal femur which has been telescoped. The affected cartilage is aplastic, irregularly calcified, vascular and cystic (Porak and Durante, 1894; Harris, 1933). Vascular fibrous bands partially separating the epiphysis from the metaphysis were present. Harris regards the mucoid degeneration of the cartilage, well seen in the distal epiphysis of the femur, as the underlying feature of achondroplasia.

Degeneration of cartilage

FIG. 104.—Achondroplasia. Skiagram of legs, showing short, massive femora and tibiae, with "mushrooming" of extremities at knees.

(4) Clinical picture

The appearance of the achondroplasiac is even more striking at birth than in later life, the relatively large head and peculiar facies sometimes leading to a diagnosis of hydrocephalus or cretinism. (The latter mistake should not be made, as the signs of cretinism are not present at birth.) In those that are still-born the trunk is sometimes grossly shortened, though in those that survive it is relatively little affected, apart from a constant lordosis. The achondroplasiac develops into a short-limbed dwarf, with waddling gait due to tilting of the pelvis and curving of the long bones of the legs, and hands which barely reach to the gluteal folds. The fingers are short and widely divided (trident hand).

Short-limbed dwarf

Sexual development and fertility are normal, though females can rarely bear living children except by Caesarean section owing to contraction of the pelvis and thickening of the iliac crests.

The intelligence and muscular development of achondroplasiacs is usually normal, and many find occupation as circus clowns. It is said that they frequently compensate by becoming vicious and bad-tempered.

(5) Prognosis

Whereas many achondroplasiacs are still-born or die within the first few days, those that survive are usually healthy and have a normal life-span.

(6) Diagnosis

The appearance of the short-limbed dwarf with head of normal size and depression of the nasal bridge is entirely characteristic. Confirmation of the



Fig. 107. — Chondro-osteodystrophy (Morquio's disease), showing deformities of thorax and spine and flexion deformities of limbs.

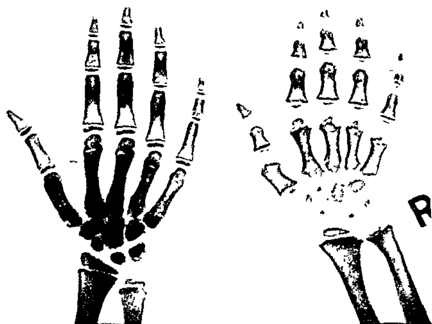


Fig. 108.—Chondro-osteodystrophy. Skiagram showing irregularity and fragmentation of epiphyses, deformity of metacarpals and phalanges, and wide joint spaces, compared with normal control of same age.

(2) Aetiology

Arachnodactylia occurs in both sexes, and is frequently hereditary or familial. Ectopia lentis may either appear in association with the skeletal deformities, or both arachnodactyly and ectopia lentis may appear separately in the same families. It appears probable that conditions behave as Mendelian dominants. No other aetiological factor is known.

(3) Clinical picture

Many of these patients come under observation on account of defective vision due to ectopia lentis, and it is only when the association is known that the minor degrees of arachnodactylia are recognized. The dislocated lenses may be opaque, and Hudson (1932) has found them resistant to absorption.

In the more severe cases, patients are above the average height, owing to the length of the lower extremities, but are remarkably thin and commonly show postural deformities. These are increased by the laxity of the ligaments; pes planus and hammer-toe are common. Other deformities of the skeleton (*Trichterbrust*, pigeon-breast and spina bifida) may occur in association; the skull is commonly dolichocephalic, and the orbital ridges may be prominent and the jaw prognathous. Congenital morbus cordis is present in about one-third of cases; webbing of the fingers, deformities of the ears, and poorly developed musculature are frequently seen (*see* Fig. 106). Respiratory infections are common, and a number of the reported cases have died from pneumonia. Radiologically, the length and slenderness of the extremities, particularly the metacarpals and metatarsals, are well seen, but apart from this the radiological changes are not characteristic and ossification is normal for age. In three instances, the association of fragilitas ossium has been noted.



FIG. 106.—Arachnodactylia. The fingers are extremely long and slender for the age (7 years) and show partial webbing. The patient also had bilateral ectopia lentis and congenital morbus cordis; the father had arachnodactylia and ectopia lentis.

(4) Treatment

Treatment is directed to relief of the deformities, such as pes planus, kyphosis and scoliosis.

5. CHONDRO-OSTEODYSTROPHY

(Brailsford–Morquio syndrome; Morquio's disease; osteochondrodystrophia deformans)

This condition, which shows a strong familial tendency, was described by Brailsford (1929) and by Morquio (1929). Whilst the most severely affected

literature the condition is sometimes known as Hurler's disease (1919) or dysostosis multiplex typus Hurler. The bony changes are probably allied to those described by Brailsford and by Morquio, since there is some evidence that gargoylism and chondro-osteodystrophy may occur in the same family groups, but there are certain differences. Thus in gargoylism the skull is affected, showing hydrocephalus and hypertelorism, and the bodies of one or more lumbar vertebrae show a constant and characteristic deformity. The superior and anterior quadrant of the affected vertebral body is missing, giving an anterior hook-like silhouette and causing angular kyphosis (*see* Fig. 109).

Hook-like lumbar vertebral body

6. CRANIAL DYSOSTOSES

A large variety of congenital cranial malformations have been described, occurring alone or in association with other skeletal or visceral deformities. The literature is confused, owing to the number of names that have been applied to different forms, some of which have the same underlying pathology.

(1) Brachycephaly and dolichocephaly

These occur as racial characteristics, but the former is seen in an extreme form in mongolism and the latter in association with arachnodactylia.

(2) Microcephaly

This occurs as a familial deformity associated with cerebral aplasia and mental defect. There is premature synostosis of the cranial bones, resulting in a greatly reduced cranial capacity, but it is probable that the premature synostosis is the result and not the cause of the small size of the brain.

(3) Plagiocephaly

This is a term applied to cases of asymmetrical cranial synostosis, but as at least the majority of these cases are examples of acrocephaly, the distinction does not appear to be a valid one.

(4) Hypertelorism (Grieg, 1924)

This is characterized by wide separation of the eyes due to gross overdevelopment of the lesser wing of the sphenoid. There is no premature synostosis. Abernethy's report (1927) of an affected family indicates that the condition is inherited as a Mendelian dominant, and whereas a number of the cases described in the literature showed mental defect, this is by no means necessarily present. It is probable that minor degrees of the deformity are much commoner than the literature would suggest. A similar separation of the eyes may occur secondarily to raised intracranial pressure in hydrocephalus, or to the deformity in oxycephaly.

(5) Fenestrae parieteles symmetricae (congenital parietal foramina)

These occur as a heredo-familial abnormality, transmitted as a Mendelian dominant. Symmetrical foramina from ½ to 5 centimetres in length and 1 to 2 centimetres in width are found in the parietal bones, situated near the posterior and middle thirds of the sagittal suture (Halbertsma, 1940); their feel resembles that of the anterior fontanelle in infants, and the pulsation of the dura can be appreciated through them. They are usually symptomless, and if their nature is recognized are of no clinical significance.

patients die in early infancy, milder cases may survive to adult life. The clinical picture is characteristic, the patient being a mis-shapen dwarf with the head apparently telescoped on to the kyphotic trunk. The dwarfing is accentuated by the flexion deformities of the extremities which are often present, and by the prominent sternum and deformed thorax (*see* Fig. 107). The face and skull are usually unaffected, and the mentality is normal. Radiologically, there is gross irregular deformity of both the long bones and epiphyses, with great increase in the joint spaces. The epiphyses of long bones and surfaces of vertebral bodies show irregular ossification proceeding from multiple nuclei,

Spinal and thoracic deformities

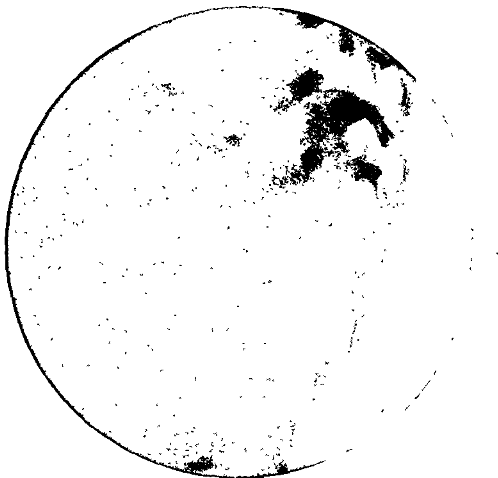


Fig. 109.—Gargoylism. Skiagram of spine showing hook-like deformity of body of lumbar vertebra.

or apparent fragmentation. The intervertebral spaces are correspondingly irregular and enlarged (*see* Fig. 108).

Allied syndrome: Gargoylism

Under this title Ellis, Sheldon and Capon (1936) described 7 cases showing chondro-osteodystrophy, corneal opacities, hepatosplenomegaly, mental deficiency, and a peculiar and characteristic facies, adding 10 others from the literature. They suggested that the condition might prove to be one of lipoidosis, and this has since been shown to be the case. The first published description appears to have been that of Hunter (1917), though in the continental

modifying genes occur. Park and Powers (1920) and Ferriman (1941) regard the underlying pathology as essentially an aplasia, the factor normally preventing premature synostosis at suture-lines being absent.

Clinically, the deformity and appearance of the skull will depend upon the site of the synostosis. Thus when it occurs at the site of the coronal and lambdoidal sutures the skull is oxycephalic, at the sagittal suture, boat-shaped (scaphocephalic), and at the metopic suture, trigonocephalic (Ballantyne, 1938). The oxycephalic skull is typically raised almost to a point or crest anteriorly, with pushing forward of the anterior fontanelle, which may remain patent. The eyes show a degree of exophthalmos which in advanced cases is extreme, and associated with optic atrophy and sometimes corneal ulceration. The raised intracranial pressure also gives rise to severe headache, and fits occur in some cases. Anosmia is frequent. In most cases the mentality is normal, but mental deficiency is sometimes present. Psychoses (Weygandt, 1921) and endocrine disturbances and dwarfism (Gunther, 1930) have been described.

Headache; mental state

Radiologically, the skull usually (but not invariably) shows well-defined digital markings, and obliteration of the suture-lines at the site of synostosis. Aplasia and synostosis at the base of the skull, enlargement of the sella turcica, and "basilar lordosis" have been described (Bertolotti, 1910).



Fig. 112.—Craniofacial dysostosis. Patient shows extreme exophthalmos and hypoplasia of mandible in addition to towering skull.

(*a*) *Craniofacial dysostosis*

Craniofacial dysostosis was described by Crouzon (1912) as a separate disease and is known by his name. There appears little doubt, however, that cases in which the peculiar facies occur —hypoplasia of the maxilla with relative prognathism of the mandible, parrot-beak nose, high-arched palate—are in other respects identical with acrocephaly and represent a manifestation of that disease (*see* Fig. 112).

Treatment.—The treatment is palliative in the advanced cases. In early cases with normal vision or early papilloedema, surgical relief of intracranial pressure has been attempted to save vision.

(*b*) *Associated syndromes: Acrocephalosyndactyly*

(i) *Acrocephalosyndactyly* (Apert, 1906).—This is a rare condition of which about one-third of the reported cases have been familial, and in which acrocephaly is associated with webbing of the fingers and toes, complete or partial syndactyly, or even ectrodactyly, and other changes in the bones and joints of the extremities. Ferriman (1941) considers the disease is closely related to



FIG. 110.—Cranio-cleido dysostosis. Radiograph showing dysostosis of skull.

(6) Lacuna skull

Multiple fenestrations of the skull, separated by thickened bridges of bone, are seen in the parietal, occipital or frontal regions in some cases of spina bifida and meningocele. Rarely they occur as an isolated phenomenon (Dorrance, 1940).

(7) Cranio-cleido dysostosis (Marie and Sainton, 1897)

This is a type of dysplasia in which the vault and base of the skull and clavicles are principally affected. The condition occurs in both sexes, and is heredo-familial, having in some instances been traced through four generations.

Clavicles and skull

Owing to the partial or complete aplasia of the clavicles, the shoulders can be approximated anteriorly; the cranial deformities include prominence of the frontal regions which are separated by a gutter, persistent patency of the fontanelles, and presence of Wormian bones in the skull (*see* Fig. 110). The maxilla is hypoplastic, with relative prognathism of the mandible. Dentition is delayed and defective, the first dentition sometimes being retained into adult life. In addition, the skeleton as a whole may show retarded development, and postural and thoracic deformities are common.

Pubic bones

Partial or complete aplasia of the pubic bones is a frequent association (*see* Fig. 111).

(8) Acrocephaly (hypsicephaly; steeple skull; stenocephaly; tower skull; turricephaly)

Exophthalmos and optic atrophy

A condition of premature synostosis of the bones of the skull, resulting in raised intracranial pressure, a crested, *casque de pompier*, or towered deformity of the cranial vault, exophthalmos, and optic atrophy. The condition is almost certainly transmitted as a Mendelian dominant, and careful examination of members of affected families will frequently bring to light mild or early cases which have not progressed to cause optic atrophy. There is, however, some evidence for supposing that



FIG. 111.—Radiograph of pelvis of same patient, showing absence of pubis.

from the diaphyseal extremities, and later as bony tumours or osteochondromas with coarse trabeculation and foam-like appearance; the lesions in dyschondroplasia, on the other hand, are seen as gaps in the ossification of the affected bones.

In diaphyseal aclasis (*see* Fig. 113) the exostoses arise from the diaphyses, and it has been suggested by Keith that the factor which controls the normal moulding of the contour of the diaphysis is at fault. Membrane bones are not affected. From their proximity to the epiphyses, and the large size they may attain, multiple exostoses are liable to cause considerable deformity; very rarely they may become sarcomatous. Shortening of the ulna may result in bending of the radius; pseudo-arthrosis is often seen (*see* Fig. 114).



Faulty moulding of diaphysis

Fig. 114.—Skiagram of diaphyseal aclasis.

Owing to their multiplicity and the general progress of the disease, particularly during childhood, removal of individual exostoses is likely to result in little permanent benefit, but this procedure may be indicated when pressure symptoms are occurring in neighbouring nerves or arteries. In some cases there is spontaneous arrest after puberty.

Indications for excision

8. DYSCHONDROPLASIA (OLLIER)

(Ollier's disease)

Although this condition is sometimes referred to as multiple chondromas, the description is not accurate. Hunter and Wiles (1935) define it as a disease of the growing ends of bone in which the normal ossification of cartilage fails to take place, so that, as the bone increases in length, there remain in the diaphyses areas of cartilage which do not ossify (*see* Fig. 115). There may in addition, however, be overgrowth of cartilage, particularly when the condition affects the hands. In most cases, symptoms occur in childhood and the condition is generally regarded as congenital. Unlike diaphyseal aclasis (with which dyschondroplasia has frequently been confused), the condition

Symptoms

acrocephaly and due probably to disturbance in an allelomorphic gene and also transmitted as a Mendelian dominant.

(ii) *Acrocephaly with atypical chondro-osteodystrophy.*—Acrocephaly with atypical chondro-osteodystrophy may occur, the relationship to both diseases being obscure.

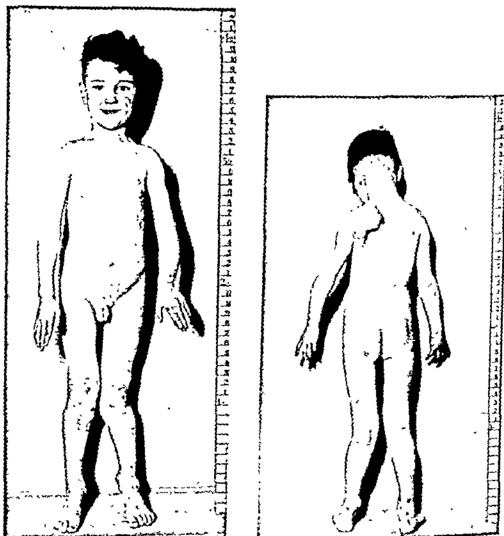


FIG. 113.—Multiple exostoses (diaphyseal aclasis) in a boy.

7. DIAPHYSEAL ACLASIS

(Hereditary deforming chondrodysplasia; hereditary multiple exostoses; multiple congenital osteochondromas)

This condition has been described under a large number of titles, and there is much confusion in the literature between true diaphyseal aclasis (Keith, 1919), which is heredo-familial and has been described as a Mendelian dominant in three and four generations, and the condition of dyschondroplasia described by Ollier where there is no evidence of a hereditary factor. Brailsford (1944) also draws a distinction on radiological grounds, since in diaphyseal aclasis the exostoses are seen in the infant as bony buds projecting

from the diaphyseal extremities, and later as bony tumours or osteochondromas with coarse trabeculation and foam-like appearance; the lesions in dyschondroplasia, on the other hand, are seen as gaps in the ossification of the affected bones.

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Symptoms

described by Ollier (1899) shows no familial or hereditary tendency. The differential diagnosis from diaphyseal aclasis has already been discussed, but it might appropriately be said that the two differ as chalk from cheese—in diaphyseal aclasis the trumpet-shaped expansion of the long bones and exostoses are calcified, whereas in dyschondroplasia the affected portions of the bones and excrescences consist primarily of radio-translucent cartilage, and calcification is minimal in the early stages. Later, calcification may be more in evidence. The general outline of the shaft usually is unaffected, or shows only slight fusiform expansion. Hunter and Wiles found 29 strictly unilateral, and 10 almost entirely unilateral, cases described in the literature, and considered that the number of bilateral cases would not exceed this number. Facial asymmetry was also a feature of 6 of the unilateral cases.

Differentiation from diaphyseal aclasis

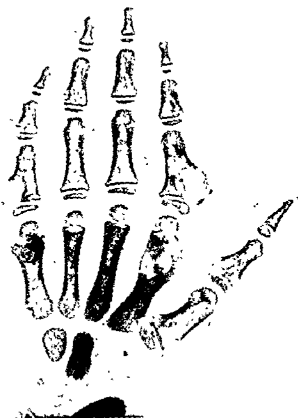


Fig. 115.—Skiagram of Ollier's disease. (*By courtesy of Sir Thomas Fairbank.*)

Symptoms will depend upon the site of the lesions. Shortening of an affected limb may occur, and if the hands are involved, the gross cauliflower-like excrescences on the fingers cause great deformity and interference with function. It is probable that cases described as multiple systematized enchondromas are in fact examples of dyschondroplasia. Pain is sometimes complained of, but it is not necessarily severe. Bending of the lower limbs is likely to occur when these are affected, and fractures are not very uncommon, but unite well. The prognosis as regards life is usually good, though there is evidence that the cartilaginous areas may sometimes become sarcomatous in adult life.

Prognosis

Treatment

Treatment is along general orthopaedic lines in correcting deformities, but is ineffective in influencing the progress of the disease.

9. MELORHEOSTOSIS (LÉRI)

(Osteopathia hyperostotica; osteosclerosis; osteosis eburnans monomelica)

Léri and Joanny (1922) described a condition of hyperostosis of the bones of one limb, in which in the appearance resembled candle-drippings running

down the shaft. The disease is rare, and the lesions almost always limited to the bones of a single limb (*see* Fig. 116). Hall (1943), who reported an atypical case associated with tuberous sclerosis, has reviewed the literature, and concludes that the condition is a local disorder of osteogenesis, characterized by periosteal deficiency and a spread of ossification from the affected bone into adjacent tissues (*see* Fig. 117). In numerous instances, the skin of the affected limb has appeared in some way abnormal, showing scleroderma, trophoedema, erythema and varicosities. In one case (Gillespie and Siegling, 1938) the limb had been x-rayed in early infancy on account of generalized induration of the soft tissues, and the bone found normal at that time, though typical melorheostosis subsequently developed. Whereas the joint surfaces are unaffected, there may be limitation of movement due to adjacent hyperostosis and involvement of the soft tissues, and when the fingers are affected they show considerable swelling and deformity.

Signs

Skin abnormalities



FIG. 116.—Melorheostosis. Right foot showing characteristic lesions (only the right lower limb was affected). (*By courtesy of Mr. R. H. Boggon.*)

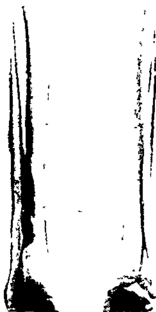


FIG. 117.—Melorheostosis, showing appearance of "candle-drippings" along shaft of right fibula. (*By courtesy of Mr. R. H. Boggon.*)

Clinically, apart from the appearance of the skin, the most common symptom is pain. When a lower limb is affected there is often limping and occasionally there is actual shortening of the limb.

Symptoms

Deformities should be corrected, but no general treatment has been found effective, and the aetiology of the condition is unknown.

10. OSTEOGENESIS IMPERFECTA

(Brittle bones and blue sclerotics; fragilitas ossium; Durante's disease; Lobstein's disease; osteopsathyrosis)

A condition of extreme fragility of the skeletal system, resulting in

Blue sclerotics and otosclerosis

multiple fractures and deformities, associated in some cases with blue sclerotics and otosclerosis. It was previously customary to distinguish the foetal form, in which fractures occur *in utero* and the infants seldom survive more than a few days or weeks, from the type in which fractures first occur during childhood. The main reason for doing so appears to be that the foetal cases are seldom



FIG. 118.—Osteogenesis imperfecta. Radiograph of skeleton of newborn infant showing multiple fractures of ribs, long bones, etc.

familial or show blue sclerotics, whereas the childhood type shows a strong heredo-familial tendency and is commonly associated with a peculiar slaty-blue colour of the sclerotics. Patients or other members of their families may also be affected with otosclerosis. In spite of this, however, it is now usually considered that the two types are different manifestations of the same disease.

When the condition is seen in the new-born, the infants show gross deformities of the limbs due to fractures during birth or *in utero*; the intra-uterine

fractures may have healed with callus formation (*see* Fig. 118). The skull feels like parchment, and radiological examination shows the presence of innumerable Wormian bones. Except in the cortex, ossification of long bones has not advanced beyond calcification of the cartilage (Brailsford, 1944). Many such infants are still-born, others surviving for a short time only.

The childhood cases vary greatly in severity, but all show a tendency to fracture on trivial injury. The fractures heal with prolific callus formation, but when multiple fractures have occurred (and these may number from 20 upward) some degree of deformity is inevitable. In the severest cases this may be very gross and result in extreme dwarfing. Patients who are less affected tend to be slender and poorly developed, and show a general laxity of ligaments, but in some cases there is slight improvement after puberty. The skull commonly shows lateral bulging above the ears, as though it had been pressed downward from the vertex. *Dwarfing*



Fig. 119.—Osteogenesis imperfecta. An adult patient showing extreme dwarfing due to multiple fractures of limbs and spine.

Radiologically, the condition is recognizable in older patients from the slenderness of the long bones, which may appear relatively expanded at their extremities, and the presence of multiple old fractures (*see* Fig. 119). Brailsford describes irregularity of the metaphyseal borders appearing with the approach of puberty, and excavations into the diaphyseal and epiphyseal bone. The shafts show great reduction in cancellous tissue, though this appears as an open meshwork at the extremities.

Diagnosis is readily made in the presence of a family history, blue sclerotics, and a history of multiple fractures. In the new-born, the condition has sometimes been mistaken for foetal rickets, particularly when multiple fractures of the ribs have produced pseudo-beading, whereas subperiosteal haemorrhages may simulate infantile scurvy. Careful examination, however, should demonstrate the nature of the deformities; skiagrams of the long bones show no rachitic changes, whilst the appearance of the skull is characteristic. *Diagnosis*

In spite of an extensive literature (which has been reviewed by Fulconis, 1939) and numerous investigations and necropsies, the aetiology remains obscure. Apart from the immediate treatment of fractures, no treatment has been found effective in modifying the disease.

11. OSTEOPATHIA CONDENSANS DISSEMINATA

(Osteopoikilosis; osteopecilia; spotted bones)

This condition was described in 1915 by Albers-Schönberg, and though it bears no obvious relationship to osteopetrosis it is sometimes, confusingly,

also known as Albers-Schönberg's disease. It is symptomless, and the condition is usually *discovered accidentally* when patients are x-rayed for some other cause. The radiological picture is characterized by round or ovoid areas of condensation scattered throughout the spongiosa of the affected bone and linear streaking along the shaft; any part of the skeletal system may be affected. The condition is congenital and may be familial and hereditary. The aetiology is otherwise unknown, and in the absence of symptoms, no treatment is indicated.

12. OSTEOPETROSIS

(Albers-Schönberg's disease; chalky bones; congenital osteosclerosis; marble bones; osteosclerosis fragilis generalisata)

(1) Definition

Anaemia—pressure on cranial nerves

A congenital disorder of calcification of bone, in which increased sclerosis of both long bones and membranous bones results in encroachment on the medullary cavity with resultant anaemia, and in pressure on cranial nerves. The condition was first described by Albers-Schönberg in 1904, since when between 40 and 50 cases have been added to the literature.

(2) Aetiology

The condition is congenital and frequently familial; direct inheritance from an affected parent, either from mother (Pirie, 1930) or father (Ghormley, 1922), has been described, and although consanguinity of parents has been recorded in several instances, it is unlikely (in view of the cases of inheritance from an affected parent) that the condition will prove to be of a simple Mendelian recessive character. Both sexes are affected. The theory of aetiology for which there is at present most support is that advanced by Dupont (1930), who postulated *parathyroid hyperactivity* in view of the finding of a parathyroid adenoma in the case of Péhu, Policard and Dufourt (1931). Whereas Parathormone injection is known to produce mobilization of calcium from the bones and osteoporosis in the first instance, Pugsley and Seelye (1933) have shown that in rats prolonged injection may result first in an osteoclastic reaction (osteitis fibrosa) followed later by an osteoblastic reaction with the production of a condition closely resembling osteopetrosis.

(3) Surgical anatomy and pathology

The distribution of the osseous sclerosis is symmetrical, and both long bones and membranous bones are affected. In the former, it is usually *seen first* at the extremities and progresses towards the centre; in the skull, the base is first affected; the carpal bones, in the early stages of the disease, appear heavily ringed. In advanced cases, radiological examination shows an almost uniform dense opacity, with loss of bony structure and obliteration of the medullary cavity. The extremities of the long bones and the clinoid processes may be clubbed. Dupont has claimed that the sclerosed bone is harder than normal and that fractures occur through lines of rarefaction, and the skiagram (*see* Fig. 120) here reproduced shows well-marked vertical lines of rarefaction at the lower end of the femur and distal end of the tibia. Pirie, however, found that the opaque bone was of the consistency of chalk and could be broken and drilled in the same manner.

Fractures

With the encroachment on the medullary cavity, a progressive anaemia develops and is associated with splenomegaly and glandular enlargement. Pressure on cranial nerves at the base of the skull results in nerve palsies and ultimately optic atrophy.

Evidence of abnormal calcification outside the osseous system may be found, such as renal calculi (Péhu, Policard and Dufourt, 1931), and calcium deposits in the tendons and myocardium (Schulze, 1921) or blood-vessels and skin (Alexander, 1923). Serum-calcium estimations have been normal except in two instances, in which hypercalcaemia has been described. The finding of a parathyroid adenoma in one case has been mentioned.

(4) Clinical picture

The condition may be recognizable radiologically at birth or even *in utero*, but patients frequently do not come under observation until considerably later unless an older child has been affected. The first symptom is usually fracture of an affected bone, and though healing proceeds normally without excessive callus-formation, recurrent fractures are common. In severely affected cases, optic atrophy and cranial nerve palsies may occur within the first year of life. Dentition may be delayed, and the teeth when they erupt appear defective or chalky.



FIG. 120.—Osteopetrosis (Albers-Schönberg's disease). Skiagram showing dense sclerosis and obliteration of medullary cavity, with fractures of femur and longitudinal lines of rarefaction at distal end of femur and proximal end of tibia; characteristic expansion of both bones. (From a male infant aged 18 months; an older brother had died with "anaemia, large liver and spleen"; parents unrelated.)

The occurrence of anaemia with the progressive destruction of the bone-marrow is characteristic. Enlargement of the spleen, liver and lymph glands represents an attempt at compensation for the loss of bone-marrow, but the anaemia, which is of myelophthisic type (Boyd, 1931), ultimately becomes aplastic and proves fatal. In the earlier stages, reticulocytes and nucleated red cells may appear in the circulation from overactivity of the remaining bone-marrow. *Anaemia*

(5) Diagnosis and differential diagnosis

The diagnosis rests on the radiological appearance of the sclerosis, which is denser, more symmetrical and more widespread than in any other condition, and is confirmed by the appearance of anaemia (with hepatosplenomegaly) and cranial nerve palsies. The contour of the long bones may be expanded, but remains smooth and quite unlike the appearance seen in melorheostosis Léri. In typical cases, where the sclerosis appears first at the ends of the long bones and progresses towards the centre of the shaft, the diagnosis should be clear, but where the site is atypical, the radiological appearance may be confused with that of osteogenesis imperfecta tarda. It is possible that the two conditions are in fact related, and that intermediary forms occur (Ellis, 1934); they are sometimes grouped together as two types of fragilitas ossium.

(6) Treatment

Up to the present time, no method of treatment has been found effective, but if the theory of parathyroid overactivity is confirmed, parathyroidectomy would appear a rational procedure.

Figs. 107 and 108 are reproduced from "Infantalism and Dwarfism" in *Index of Differential Diagnosis of Main Symptoms*, edited by French, H. and Douthwaite, A. H., published by John Wright and Sons, Bristol. Sixth edition, 1945.

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BONES—METABOLIC DYSTROPHIES

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1. CALCIUM METABOLISM

68.] The metabolism of calcium is closely linked with that of phosphorus, so that changes in one are often secondary to changes in the other. A reciprocal relationship exists between the levels of calcium and of phosphorus in the blood.

(1) Normal calcium metabolism

The digestive processes convert all the calcium in the food into its inorganic salts but calcium is nevertheless absorbed with difficulty, and an excess of it in the diet is to be desired. The daily requirement for adults is between 0·4 and 1·0 gramme, and in children and pregnant or nursing women it is higher. Absorption is assisted by vitamin D, and hindered by excess of certain mineral constituents.

Calcium requirements

Excretion of calcium salts is primarily by way of the large intestine, so that faeces contain the unabsorbable residue plus that which is excreted. Elimination also takes place through the kidneys, and increases with acid-forming diets.

Excretion

In blood, calcium is found to be absent from the corpuscles, whereas in the plasma there is more than in the serum. Many of the methods of estimation are open to criticism, but the best give normal limits of 9–10 milligrams, expressed per 100 cubic centimetres of serum. Phosphorus is equally distributed in blood constituents, and is usually expressed as milligrams per 100 cubic centimetres of plasma, normal limits being 2·5–3·5 milligrams per 100 cubic centimetres in adults, and up to 5 milligrams in children. The serum-calcium figure tends to be low in pregnancy, a in a child while it is suckling.

Blood chemistry

Normal values

Phosphatases appear to be needed wherever in the body active calcium metabolism is taking place. They are present in the intestinal mucosae, in kidney, and in parts of bone, particularly in children. Plasma also contains phosphatase, which can be measured in terms of the number of milligrams of phosphorus which 1 cubic centimetre of plasma will liberate from sodium β-glycerophosphate in 48 hours at 38° C., and at *p*H 7·6. The normal value is 0·15 milligram which may rise considerably in certain bone diseases. *Phosphatases*

The skeleton, besides being strengthened by calcium salts, acts as a reservoir for these salts, upon which the body can draw in times of dietary shortage, and to meet the demands of the foetus or of lactation; serum-calcium levels must at all times be maintained to ensure coagulability of shed blood, and normal irritability of muscle and nerve, though it is surprising that levels as low as 6 milligrams or as high as 19·8 milligrams have been observed in conditions of disease, yet no specific symptoms were caused. *Functions of calcium*

(2) Effects of dietary deficiencies on calcium metabolism

Vitamin C plays an important part in the ossification of bone; without it there is no activity of the osteoblasts, but in spite of this, calcium metabolism remains normal and indeed the zone of provisional calcification is thicker and less regular than usual. Clinically, the result of vitamin C deficiency is scurvy. *Vitamin C deficiency*

After the work of Mellanby (1918) on antirachitic propensities of oils and fats, it was discovered that ultra-violet irradiation had a similar effect, and finally pure calciferol was isolated. Thus vitamin D and calcium and phosphorus metabolism were linked together. Without vitamin D inorganic phosphorus salts cannot be properly absorbed from the intestinal mucosae, nor can they be deposited in the osteoid seams of bone. Such, in fact, is the pathogenesis of rickets and osteomalacia; for osteomalacia *is* adult rickets. It is equally likely that poor absorption of vitamin D, as seen in coeliac rickets and idiopathic steatorrhoea of adults, causes a secondary calcium deficiency leading to low serum calcium and tetany. *Vitamin D deficiency*

During fasting, calcium is continuously excreted from the skeleton. In animals on a diet poor in calcium the trabeculae of spongy bone become diminished. Calcium deficiency in the diet is at least one factor in producing osteomalacia. It commonly starts in a period of lactation when calcium is drained from the skeleton, and in women of countries where the daily intake of calcium is inadequate. War may produce a like deficiency of calcium and all other essentials in the diet, and the result is hunger osteopathy, clinically similar to osteomalacia. *Calcium deficiency*

Phosphorus deficiencies are not seen in human medicine, but cattle in certain parts of South Africa show an osteomalacia-like disease called *styfsiekte*, or "stiff-sickness". Experiments have shown that this is due to phosphorus deficiency.

(3) Effects of parathyroid hormone and thyroxine on calcium metabolism

Phosphorus and calcium metabolism are specifically affected by the parathyroids. Removal of these glands in men and animals results in a low serum-calcium level, while injection of a glandular extract such as Parathormone raises the level above normal, but these effects of Parathormone on calcium *Action of parathyroids*

levels are probably secondary to changes in phosphorus metabolism. The hormone rapidly increases the excretion of phosphorus and its level in the blood falls; owing to the reciprocal relationship between blood phosphorus and calcium, the level in the serum of the latter must rise, and to allow of this the bones yield up calcium. Finally, the raised serum-calcium level causes excess calcium to be excreted into the urine and a drain of calcium is established from skeleton to urine (Fig. 121). On administering Parathormone, the increase in calcium excretion lags behind that of phosphorus, and when the administration is stopped phosphorus excretion returns abruptly to normal, to be followed

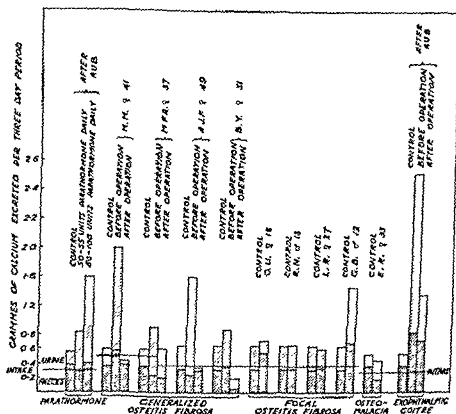


FIG. 121.—Calcium-balance estimations in various diseases involving bones. Calcium excretion was estimated on a low calcium diet of approximately 100 milligrams daily as shown by the horizontal lines. Urinary calcium excretion is represented by single cross-hatching. The first 3 columns show the effect of injecting Parathormone into normal individuals.

later by the calcium excretion. Such alterations in excretion affect the urinary, far more than the faecal, output. This chain of events suggests where the pathogenesis of generalized osteitis fibrosa lies, for in this disease the increased secretion of hormone from a parathyroid tumour produces the very same effects. It must be noted that normal individuals respond very variably to Parathormone, and injections of it may significantly raise the urinary calcium excretion without necessarily causing a hypercalcaemia.

Action of thyroid

In hyperthyroidism and also in normal persons given thyroid extract or thyroxine, calcium excretion is increased out of proportion to any rise in the basal rate of metabolism. This action is greater than that of Parathormone, and yet the serum calcium is unchanged. Moreover, it is in hyperthyroidism

that there is a distinct increase in faecal as well as in urinary calcium excretion. Thyroxine probably does not directly stimulate the parathyroids, otherwise the serum calcium would rise; nor can a general increase in metabolic activity adequately explain the facts, because there is no increased output of calcium in fevers or leukaemias when metabolism is increased without thyroid disease. So thyroxine may perhaps directly increase bone katabolism. It has been found that somewhat less than 50 per cent of cases of hyperthyroidism have demonstrable osteoporosis as a result of increased calcium loss (Hunter, 1930). In this disease plasma-phosphatase values are often high. In myxoedema, conversely, the rate of excretion of calcium is subnormal, and can be restored when thyroid is administered.

(4) Methods of the metabolism ward

In studying calcium metabolism it is necessary to know, not only the blood levels of calcium and phosphorus, but also the calcium and phosphorus balance; for the direction in which a river flows is not be to found simply from its level. *Calcium balance*

A calcium-balance estimation can best be made with the patient in a ward under the care of a painstaking Sister-Dietician. Because salt-excretion levels only become constant slowly, it is best not to change the conditions of study more than once in 12 days. A diet low in calcium is needed to reduce to a minimum the unabsorbed calcium in the faeces. The daily intake is fixed at *100 milligrams* by allowing the patient to choose a palatable dietary from a list of foods low in calcium content. This diet must then be adhered to throughout. Fluid and sodium chloride intake is also kept constant, and distilled water is used in the preparation of all the food and drink. Liquid paraffin may be needed as a laxative, and the urine is kept neutral to phenolsulphonphthalein (*p*H 7·3) with sufficient sodium bicarbonate by mouth. The faeces are divided into 3-day periods by oral administration of 0·3 gramme of carmine alum lake taken every third day. This marker should appear in the stools within 24 hours on each occasion. The total faeces passed in the period are collected for calcium estimation, and so is the corresponding urine sample, in 24-hour specimens over the same 3-day period. After a preliminary 3-day trial on the prescribed diet, excretion is estimated usually for the next 2 periods of 3 days each. The normal figures under these conditions should be about 185 milligrams of calcium in the urine and 385 milligrams in the faeces. *Method* *Normal values*

2. GENERALIZED OSTEITIS FIBROSA

(1) Definition and aetiology

This disease is otherwise known as hyperparathyroidism or osteitis fibrosa of von Recklinghausen. It is due to excessive secretion of parathyroid hormone from either hyperplasia or neoplasm of these glands. Its features are (1) hypercalcaemia, (2) negative calcium balance and (3) decalcification of the skeleton. *Synonym*

(2) Surgical anatomy

The parathyroid glands are variable in site and number. There are usually 2 on each side, lying between the pre-tracheal fascia and the posterior aspect of

each lateral lobe of the thyroid. Aberrant tissue may be found in any part of the branchial field. The superior parathyroids are supplied by the superior thyroid arteries, lie within the capsule of the thyroid gland anterior to the pre-tracheal fascia, and may be embedded in the thyroid itself. The inferior glands are supplied by the inferior thyroid arteries; when they are in front of the pre-tracheal fascia they may enlarge downwards anterior to the common carotid artery to lie behind the sternum, but when they are placed behind the pre-tracheal fascia the latter has to be divided to expose them, and they may migrate close to the oesophagus and down into the thorax.

Location of a tumour

(3) Pathology

Bone changes

The bony changes are generalized throughout the skeleton. The cortex and spongiosa are too thin and are replaced by tough, grey, fibrous tissue, so that they cut with a knife like rotten wood. Deformities and spontaneous fractures are seen. Multiple grey, spongy osseous swellings, or round red tumours, or multilocular cysts may be present. Microscopically, lacunar resorption of bone is predominant, giving generalized osteoporosis. Apposition of new bone, however, does not cease. There is fibrosis of the marrow, and there may be osteoclastomas and cysts (Hunter and Turnbull, 1931).

Tumour

Renal calculi

Of the parathyroids there may be a single tumour, rarely tumours of 2 glands, and sometimes generalized hyperplasia of all 4. Bilateral renal calculi of calcium phosphate are commonly found. Advanced cases have shown metastatic calcification in lungs, stomach, kidneys and myocardium.

(4) Clinical picture

Women are more often affected than men. Besides symptoms related to the skeleton there are also muscular hypotonia and weakness, anorexia, nausea, vomiting and abdominal cramps and, in advanced cases, wasting. Urinary symptoms include as a rule polyuria, polydipsia, and nocturnal frequency, sometimes also renal colic and haematuria. The former symptoms result from the large quantity of water needed to excrete the excess calcium salts in the blood. When there is metastatic calcification in the kidneys the picture of chronic nephritis with renal failure and phosphorus retention may occur.

Urinary symptoms

Classical type

Skeletal signs

Occasionally the presenting features are entirely renal. However, the classical type is one with a fibrocystic skeleton, and here the skeletal symptoms predominate. There are pains in the bones, particularly in the back, pelvis and legs, deformities which slowly progress, and pathological fractures. Pelvis, spine and thoracic cage are grossly deformed, showing kyphosis, loss of total height from narrowing of the vertebral bodies, distorted ribs, and a deep antero-posterior diameter of the chest. The limbs are curved and deformed, making walking eventually impossible (Fig. 122). The teeth may be displaced or lost but are otherwise normal. The terminal phalanges may characteristically become shorter and broader than normal. From the point of view of diagnosis, such gross skeletal signs ought to be considered as very late. Anorexia and abdominal symptoms may reduce the patient to a state of cachexia.

(5) Special aids to diagnosis

(*a*) *Biochemical*

Blood chemistry

The serum calcium is raised and figures vary between 12·6 and 23·6 milligrams per 100 cubic centimetres. Values of 14 milligrams per 100 cubic

centimetres are common. Plasma-phosphorus figures on the other hand are low, varying between 1·0 and 2·7 milligrams per 100 cubic centimetres. Such figures are diagnostic, except that the plasma phosphorus may be higher when there is renal impairment. In those cases in which bone disease is demonstrable, the plasma phosphatase is raised.

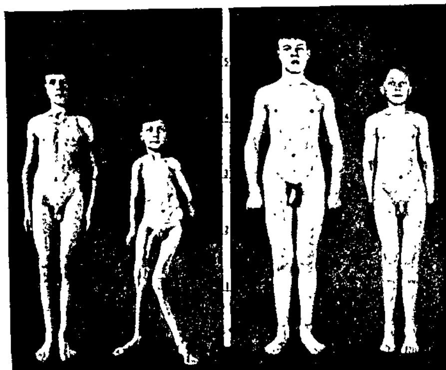


FIG. 122.—Generalized osteitis fibrosa. A boy photographed with a control of the same age when 12 years old (left) and when 15 years old (right). Osteotomy was performed on the right femur. Most of the improvement during the 3 years resulted from removal of a parathyroid tumour.

There is a negative calcium balance with a urinary excretion up to 8 times the normal; the faecal excretion is not raised unless there is renal impairment. *Calcium balance*

(*b*) *Radiological*

There is extreme osteoporosis. To demonstrate this it is necessary to take a control film, the corresponding bones of the patient and the control being exposed side by side on the same film (Fig. 123). A control should be chosen of the same sex, age, height, weight and build as the patient, and the same control ought to be employed in all subsequent skiagrams.

The cortex of bones is reduced to a thin, uneven, linear shadow, and the spongiosa loses density. The skull shows uniform miliary mottling and small cyst-like areas. The vertebrae are biconcave and reduced in height. Deformities of the pelvis in particular and of other bones are to be seen, also spontaneous fractures.

The urinary tract should be radiographed for calculi and metastatic calcification. If the parathyroid tumour is retrosternal it may throw a shadow in a chest film.

(c) *Biopsy*

In cases of great difficulty, resort may be had to a *biopsy and histological* section of bone from the tibia.

(6) Differential diagnosis

The following conditions need to be distinguished: osteomalacia, thyrotoxic osteoporosis, osteitis deformans and focal osteitis fibrosa. Reference to these



FIG. 123.—Generalized *osteitis fibrosa in a woman aged* 41 years. Skiagram shows extreme osteoporosis, thinning and bending of the bones, compared with a normal control. There is a large cystic area in the middle metacarpal causing pressure deformity of the neighbouring bones. (*By courtesy of H. K. Lewis and Co.*)

is made elsewhere in this section. The following may be confused with hyperparathyroidism: (i) senile osteoporosis and osteoporosis of disuse, (ii) osteoporosis in pituitary basophilism (Cushing, 1932), (iii) osteomalacia with renal glycosuria (the Fanconi syndrome), (iv) secondary carcinomatosis of the skeleton, (v) multiple myeloma, (vi) renal rickets, (vii) osteogenesis imperfecta, (viii) enchondromas, (ix) lipoid granulomatoses.

In only one of these conditions is the serum calcium ever raised. Cases of

multiple myeloma may show serum-calcium figures as high as 13 or even 16 milligrams per 100 cubic centimetres with a raised plasma phosphorus when renal function is impaired (Snapper, 1943). The condition is mainly distinguished on radiological evidence, in which the inner aspect of the ivory corticalis is especially picked out with clean-cut areas of complete translucence. There is Bence-Jones proteinuria in 65 per cent of cases. Osteomalacia with renal glycosuria may clearly resemble hyperparathyroidism both clinically and in skiagrams. The glycosuria is often transient, and slight albuminuria is present. In typical cases the blood chemistry of the 2 diseases is different, the serum-calcium figure being normal in osteomalacia with renal glycosuria. In both diseases the calcium output in the urine is increased. In both the plasma-phosphorus figure is low, except where the renal insufficiency of metastatic calcification of the kidneys in hyperparathyroidism interferes with the excretion of inorganic phosphate. Such cases are unusual but may lead to further confusion because of albuminuria and a drop of the serum-calcium value even to normal. *Diseases with hypercalcaemia*

In osteomalacia and renal rickets low serum-calcium levels are seen, but the other conditions described all show a normal blood chemistry. *Diseases with hypocalcaemia*

(7) Prognosis

The patient, unless operated upon, becomes bed-ridden from weakness and his deformities, and dies within a few years. There has been less than 4 per cent immediate post-operative mortality in the recorded cases, although in 10 per cent of the cases tetany or renal complications killed the patient between 19 days and 14 months after operation. *Operative mortality*

(8) Indication for surgery

Surgery is always indicated, for, though a high-calcium and high-phosphorus diet alone will improve skeletal calcification, it is contra-indicated as it increases the danger of renal calculi. Such a diet with vitamin D may be given for a few weeks prior to operation.

(9) Operative technique

The chief difficulty lies in finding the tumour. In one case (Walton, 1931) a preliminary exploration failed to show the 2 tumours, which were later found lying, respectively, retrosternally and behind the oesophagus. Sir James Walton therefore advises wide exposure through a collar incision. The sternomastoids are retracted and pre-tracheal muscles divided. The lateral lobes of the thyroid are rolled inwards to expose the normal sites of the parathyroids. If no tumour is found a finger is passed into the thorax close to the trachea; if still invisible, it may appear when the pre-vertebral space is entered by a small incision made just behind the oesophagus after the carotid sheath has been retracted laterally. Further exploration behind the oesophagus is facilitated by this incision. It is important not to mistake a small thyroid adenoma for a parathyroid tumour. After removal, the wound is closed in layers with a small tube-drain inserted in the cavity which remains. *Abnormal sites*

(10) Post-operative care

A high-calcium diet with calcium lactate (5 grammes thrice daily) is given with vitamin D and ultra-violet irradiation. Watch must be kept for the onset of tetany, and this controlled, if necessary, with intramuscular calcium *Danger of tetany*

gluconate (10 cubic centimetres of 10 per cent solution) or even Parathormone and intravenous calcium chloride (10 cubic centimetres of 5 per cent solution) in the worst cases.

(11) Results of treatment

The improvement should be dramatic. Bone pain is immediately relieved, spontaneous fractures heal quickly, and osteoclastomas often dwindle.

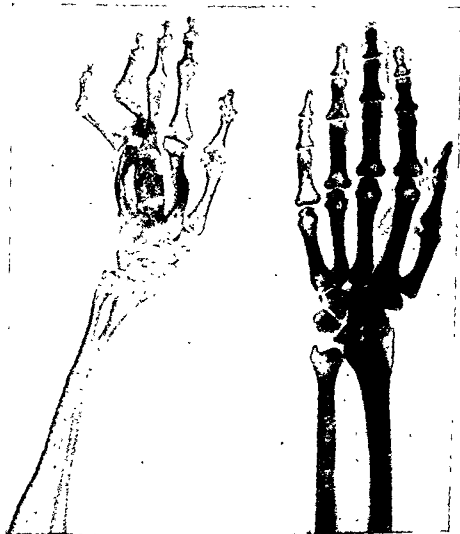


FIG. 124.—Generalized osteitis fibrosa. The same case as Fig. 123, 18 months after removal of parathyroid tumour. The bones have become recalcified and the cysts are disappearing. (*By courtesy of H. K. Lewis and Co.*)

Urinary and gastro-intestinal symptoms cease at once. The density of bones increases (Fig. 124), and the blood chemistry returns to normal or may swing over to hypocalcaemia, showing a latent or manifest tetany.

3. FOCAL OSTEITIS FIBROSA

(1) Definition and aetiology

This condition is variously known as benign giant-celled tumour, osteoclastoma, osteogenetic myeloma and myeloid sarcoma. It is a focal or

multifocal disease of bone of unknown aetiology and unassociated with any endocrine disturbance. It occurs chiefly in adolescence, and is much more common than generalized osteitis fibrosa.

(2) Pathology

Localized grey or brown tumours expand the corticalis and may form cysts. Histologically, they are of osteogenic fibrous tissue containing giant cells (osteoclasts). Apart from the local lesions, the bone is everywhere normal. *Localized*

(3) Clinical picture

The process is slow and often becomes arrested. It may be symptomless until a spontaneous fracture occurs. Deformities are seen in the multifocal variety. *Spontaneous fracture*

(4) Special aids to diagnosis

(*a*) *Biochemical*

The serum calcium and plasma phosphorus are normal; so is the calcium balance. *Generalized osteitis fibrosa can thus be distinguished at once.*

(*b*) *Radiological*

The whole skeleton is properly calcified except at the sites of the lesions, usually in the ends of the long bones, in which there is a fusiform swelling caused by a translucent cyst-like structure, traversed by a few trabeculae. The cortex is thin and expanded.

(5) Treatment

Exploration of the neck for a parathyroid tumour is quite unjustified. Treatment is for the fractures, which unite well.

4. OSTEITIS DEFORMANS

(1) Definition

Osteitis deformans or Paget's disease of bones is a chronic disease, causing enlargement and deformity of one or several bones. *It is not a generalized* disease of the skeleton. *Synonym*

(2) Aetiology

The aetiology is unknown. It is not due to an endocrine disturbance, and bears no relationship to generalized osteitis fibrosa. It is not inflammatory in origin, but may be due to a disturbance of mineral metabolism. The disease commonly starts at the age of 55 and is rare before the age of 40. Its incidence is somewhat higher in men than in women, and sometimes it is familial.

(3) Pathology

In a minority of cases one bone alone such as the tibia or the pubis may be involved. Usually many bones are affected together, and in the following order of frequency: pelvis, lumbar spine, femur, tibia, skull, clavicle, humerus, radius and rib. *Bones commonly affected*

The bones are irregularly thickened and enlarged, and are often bowed. The skull becomes very thick and its foramina are narrowed. The corticalis is broad but has lost its uniform ivory appearance, being coarse, spongy and covered with red streaks and dots. Histologically, there is evidence of increased resorption and even more of compensatory apposition of new bone. The transition between diseased and normal parts of a bone is abrupt. *Morbid anatomy*

Normal values for serum calcium and plasma phosphorus are constantly found, but that for plasma phosphatase is always above normal. The urinary calcium excretion is increased up to 4-fold in 80 per cent of cases, but the level of calcium excretion is unrelated to the clinical or radiological severity of the case.

Blood chemistry

(4) Clinical picture

The disease is always slow of onset and may be symptomless, especially in the early stages. It rarely affects the general health. The patient may complain only of increasing deformities, diminishing stature, or the need for larger sizes in hats. In 80 per cent of cases there is pain, of any type or intensity, related specifically to the bones and usually situated in the back of the legs. Headache is common. An obvious increase in circumference of the vault of the skull, compared with a normal facial skeleton in late middle life, gives an appearance which is altogether typical. Bowing of the lower limbs is common. It usually occurs in such a way as to accentuate the normal curvature of each bone. The thickening and deformity of long bones can be felt, particularly in the tibia. Rarely, encroachment of expanding bones upon soft tissues may cause compression paraplegia or cranial nerve palsies. Otosclerotic deafness is common. Spontaneous fracture is rare, but when it occurs union is rapid. Osteogenic sarcoma complicating the later stages occurs, but is not common. Arterial degeneration is to be seen in most cases, often with corresponding retinal haemorrhages and choroidal changes.

Deformities

Deafness

(5) Special aids to diagnosis

(a) Radiological

There is irregular osteoporosis, which accounts for the bending and deformities. New bone which is laid down appears radiologically in one of two forms, the spongy and the amorphous, though both may be seen in a single patient, particularly when the pelvis is involved.

Two varieties

The spongy form is the more common, and consists of irregular coarse striae both in the medullary cavity and in the corticalis, and the diameter of the bone is increased. It may have the appearance throughout of cancellous tissue highly magnified (Fig. 125). In the amorphous type the bone appears replaced by chalky amorphous shadows, and the diameter again is increased. In both forms, widening and bowing of the bones are important points in the radiological diagnosis. In the pelvis, cyst-like areas are common. In the skull the changes are irregular and affect mainly the outer table. The calvaria may be several times normal thickness, and the sutures may be obliterated. In 40 per cent of cases skiagrams will show calcified arteries.

(b) Blood chemistry

There is no significant change other than the raised plasma phosphatase which is common to several skeletal diseases.

(c) Calcium balance

This may show an increase in urinary calcium excretion.

(6) Differential diagnosis

Pulmonary osteoarthropathy is distinguished by clubbed fingers.

Carcinomatosis

Osteoplastic secondary carcinomatosis may cause confusion in the skiagrams, but in this condition there is no enlargement or bowing of the bones.

Syphilitic osteitis and periostitis, in spite of its present rarity, must sometimes be considered. There need seldom be any confusion on clinical grounds between osteitis deformans and generalized osteitis fibrosa. *Syphilis* *Hyperparathyroidism*

Differential diagnosis is more fully discussed under the latter heading.



Fig. 125.—Skiagram of the pelvis in a case of osteitis deformans of the spongy type. There is widening of the bones and alteration of the trabeculation. (*By courtesy of H. K. Lewis and Co.*)

(7) Prognosis

The average rate of progress in any bone is shown by skiagrams to be 0·5 centimetre in a year. The disease itself seldom shortens the life of the patient, who usually dies of broncho-pneumonia or from the effects of arterial degeneration.

(8) Treatment

The course of this disease is not affected by any known treatment. Ultra-violet light therapy does not increase the calcification of the skeleton. The patient is best kept on a diet of high-calcium content, that is, one containing 3 pints of milk daily, together with butter, cheese and eggs. Calcium caseinate or lactate (10 grammes a day) and a vitamin D preparation may be prescribed. *Dietary*

Iodides

For the bone pains potassium iodide has been given since the time of Paget himself. It is used as Lugol's solution, 3 minims thrice daily, increasing to 30 minims, and given in milk. Otherwise, recourse may be had to simple analgesics like aspirin, or Allonal.

Analgesics

Surgical intervention is rarely needed. Exploration of the neck for a parathyroid tumour is never justified. Rarely, osteotomies to correct deformities may be necessary, or a spinal jacket for painful kyphosis. Secondary osteoarthritis of the hip may require appropriate orthopaedic measures.

5. LEONTIASIS OSSEA

(1) Definition and aetiology

The term is now used in two senses; descriptively, when diseases such as osteitis deformans or osteitis fibrosa involve the bones of the face; and specifically, for a progressive sclerosing hyperostosis of the skull of unknown cause. The condition was once considered to be infective in origin since it may arise close to the nasal sinuses.

(2) Pathology

Although the disease does not produce a leonine expression, the connective-tissue hypertrophy of fibroma molluscum does so, and Virchow considered the two conditions analogous when he advocated the name. The disease starts in the nasal fossae and sinuses and, less commonly, at the base of the skull. There is slow growth of dense ivory bone under the periosteum, and this ultimately breaks the boundaries of the suture lines, spreading in many directions across the skull. The blood chemistry is always normal.

(3) Clinical picture

Occurring in early adult life in either sex, the disease may cause obstruction of the nose and lachrymal ducts and ultimately gross disfigurement of the whole facial skeleton. The orbit may be encroached upon, the eye protrude and optic atrophy result. There is sometimes loss of the sense of smell and of mobility of the jaws. Except in the later stages pain is unusual.

(4) Treatment

Beyond palliative removal of the grosser hyperostoses, no treatment has any permanent effect.

6. OSTEOMALACIA

(1) Definition

A generalized skeletal disease due to deficiency of vitamin D, occurring either as a primary dietary deficiency or, when seen in idiopathic steatorrhoea, as a conditioned dietary deficiency from poor absorption of that vitamin and of calcium salts. (Bennett, Hunter and Vaughan, 1932.)

(2) Aetiology

Though rare in England, the disease is endemic in Northern India and in China and Japan. It occurs sporadically in Central Europe. It is seen mostly in women in the reproductive years, often recurring more seriously with each successive pregnancy. At one time it was falsely attributed to a hyperactivity of the ovaries, but it is now certain that it is a deficiency disease resulting

Deficiency disease

usually from a combination of adverse economic factors. The oriental woman tends to be screened from the sun, to have restricted movement because of foot-binding, and to live on a diet very deficient in calcium and fats. Lactation is prolonged and repeated and, of course, represents a drain on body calcium (Maxwell and Miles, 1925). *Social factors*

(3) Pathology

Osteomalacia is adult rickets. The bones throughout are soft, they bend, and can be cut with a knife like rotten wood. Spontaneous fracture is common.



FIG. 126.—Skiagram of the pelvis in osteomalacia, showing generalized osteoporosis and deformity due to thrust of the femoral heads. The rami of the pubic bones have been severed as the result of crushing. (*By courtesy of H. K. Lewis and Co.*)

The essential abnormality is that calcification of osteoid tissue is deficient, whereas normal physiological resorption does not diminish, so that the whole skeleton is softened (Pommer, 1885).

(4) Clinical picture

Pain in the back and thighs is a predominant symptom, especially in winter. *Pain*
Extreme deformities of the pelvis, thorax or long bones develop in a haphazard way, and severe kyphoscoliosis may cause the head to sink forward on to the chest. The long bones tend to bend even more easily than they break. A waddling gait develops, which is made more apparent by general muscular weakness. Tetany is common. The typical triradiate pelvis may cause difficulty in labour often necessitating a Caesarean section. *Deformities*

(5) Special aids to diagnosis

(a) Biochemical

Hypocalcaemia Serum calcium is subnormal, being 5·0 to 7·4 milligrams per 100 cubic centimetres. The calcium balance is usually negative and can be made positive by giving the patient cod-liver oil. In cases of idiopathic steatorrhoea, estimation *Fat in stools* of fat in the stools may show total fats up to 40 per cent or more, and the bulk of this is unsplit fat. If glycerin is present the possibility of the Fanconi syndrome must be considered.

(b) Radiological

There is a variable degree of osteoporosis with accentuation of the normal trabecular pattern by contrast. In severe cases the corticalis will be a mere pencilled line in the soft tissues, with loss of bone pattern, fractures and deformities of all kinds (Fig. 126). The vertebrae are biconcave and the skull may show uneven but clear-cut areas of translucence.

(6) Treatment

Full doses of vitamin D should be given either as cod-liver oil, 2 to 4 ounces daily or as calciferol, 0·25 to 0·5 milligram daily. In addition, calcium lactate should be given by mouth, up to 10 grammes daily. Ultra-violet irradiation and a corrected dietary are needed. Improvement has resulted from ovariectomy, though the improvement probably results, not from this specific operation, but from the prevention of subsequent pregnancies. On rational grounds ligation of the Fallopian tubes should serve equally well. When pelvic deformity demands it, Caesarean section is necessary.

7. RICKETS

(1) Definition

Rickets is a nutritional-deficiency disease of infancy which affects principall; the growth of bones.

(2) Aetiology

It is due to a lack of vitamin D. This may arise in two ways (1) from deficiency in the diet of such foods as milk, butter and eggs, which contain the natural vitamin, and (2) from insufficient ultra-violet irradiation of the skin. It is seen, therefore, particularly in poor families in temperate zones. It commonly follows upon prematurity, but is less likely to attack breast-fed than artificially-fed infants.

(3) Pathology

The essential abnormality is deficient calcification of osteoid tissue, and since endochondral ossification is still going on in infancy, the zone of provisional calcification is also affected, making endochondral ossification irregular. The deficiency is generalized throughout the skeleton, and may affect any new osteoid laid down on bone which was previously well calcified.

The bones are soft and deformed, and the ends of the long bones appear *facroscopic ppearances* expanded and cup-shaped, because the region of the epiphyseal line is wider from side to side than normal. In cross-section this region shows a broad, irregular band of osteoid tissue. Bones subjected to particular stresses, such as the ribs and long bones of the legs, become bent. In the skull, there is poor

ossification of the bones of the vault with thinning and delayed closure of the fontanelle. There are frontal and parietal bosses.

(4) Clinical picture

The onset is gradual and seldom obvious before the fourth month of life. The infant is plump and develops restlessness, irritability and sweating of the head. The symptoms and signs include a general hypotonia of the muscles, laxity of the ligaments, digestive disturbances, and a mild hypochromic anaemia. The spleen is sometimes palpable and the child grows pot-bellied. The rarer cases in which the serum calcium is low may show spasmophilia. *Spasmophilia* This is a triad of signs comprising tetany (with the characteristic signs of Chvostek and Trousseau), convulsions and laryngismus stridulus, which is a crowing inspiration following spasmodic closure of the glottis.

Skeletal deformities predominate. The epiphyses show bossing and the enlarged costo-chondral junctions form the rickety rosary. The enlargement *Rickety rosary* is most obvious at the lower end of the radius (Fig. 127). The chest is deformed, the pelvis is flattened, and the long bones tend to bend. The skull is box-shaped and bossed, having a wide fontanelle. Dentition is delayed. *Skeletal deformities*

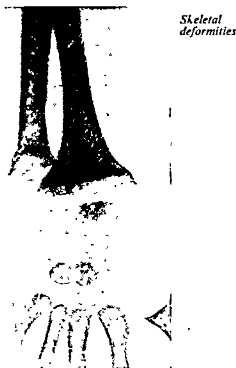


FIG. 127.—Right wrist-joint of a girl aged 2 years, showing active rickets. (*By courtesy of H. K. Lewis and Co.*)

(5) Special aids to diagnosis

(*a*) *Biochemical*

The majority of cases of rickets have a normal serum calcium, but a low plasma phosphorus. In healthy infants the figure for phosphorus should lie between 4 and 6 milligrams per 100 cubic centimetres, but in rickets it may fall as low as 2 milligrams per 100 cubic centimetres. A few cases are seen in which the phosphorus level is normal but the serum calcium is subnormal, and these children may have symptoms and signs of hypocalcaemia. A very few cases are seen with normal blood chemistry.

(*b*) *Radiological*

There is a slight but generalized osteoporosis. The characteristic changes are seen at the ends of long bones, and a skiagram of the wrists is the most useful for diagnostic purposes. The epiphyseal line is hazy, irregular and concave like a saucer or wineglass. The increased width at the epiphyseal line gives the bone an appearance of being splayed out. When healing occurs it is readily detected in skiagrams.

(6) Differential diagnosis

Rickets has to be distinguished from coeliac rickets and renal rickets. *Coeliac rickets* Coeliac rickets occurs in certain cases of coeliac disease. It is a conditioned

dietary deficiency of vitamin D, calcium and phosphorus salts, arising because the fatty diarrhoea has made absorption of these substances difficult. *Renal rickets* Renal rickets occurs in some cases of renal infantilism, and is not due to a deficiency of vitamin D, but to a disturbance of endogenous calcium and phosphorus metabolism which follows on phosphorus retention, the result of renal insufficiency. In coeliac rickets the serum calcium is constantly low, and tetany is therefore common, but the plasma-phosphorus figures are only occasionally lower than normal. In renal rickets there is a raised plasma phosphorus and the serum calcium tends to fall reciprocally, so that again tetany is common.

(7) Prognosis

Rickets is seldom fatal except where secondary complications, such as broncho-pneumonia, are encountered. Skeletal deformities seldom persist into adult life unless the condition is initially very severe or treatment is delayed beyond the third year.

(8) Treatment

Prevention is essential. During pregnancy the mother must have an adequate diet and enough sunlight. Thereafter, breast feeding is sound prophylaxis. Between the ages of 2 months and 2 years cod-liver oil, up to a teaspoonful twice daily, must be added to the infant's diet.

In the established case cod-liver oil is also given as 50 per cent emulsion, a teaspoonful thrice daily. Alternatively, a concentrate of pure irradiated ergosterol, such as Liquor Calciferolis B.P., 5 to 10 minims 3 times a day, can be used. Heliotherapy or artificial ultra-violet irradiation are valuable. To keep the child off its legs and to prevent further deformity, long lateral splints should be applied. Orthopaedic treatment will be needed later in life if the deformities persist.

8. CRETINISM

(1) Definition and aetiology

Cretinism is a condition of hypothyroidism starting in foetal life. It may occur in endemic form wherever iodine-deficiency goitre is found: rarely it may appear sporadically.

(2) Clinical picture

A goitre is often found in the endemic form of cretinism. The child is retarded in both physical and mental development. It is apathetic and dull or even completely imbecile. The total stature is below normal and the face is characteristic, with pale, thick wrinkled skin, a broad flattened nose and thick lips from which protrudes a large fissured tongue. The abdomen is protuberant, and often shows an umbilical hernia. The hair is of poor quality, the skin dry, and the dentition delayed.

In the skeletal system the fontanelles remain open for years, the centres of ossification appear late and the epiphyses fail to unite.

(3) Aids to diagnosis

Radiological

The bones are short and thick and the epiphyses are irregular, late to appear, and very slow in fusing. An extra band of density may be seen at the growing

ends of the bones; this density will extend throughout the bones unless the illness is treated adequately, *in which case it disappears. In the skull, the basal* bones are short, and ossification of the vault is slow.

(4) Prognosis

Untreated cases will remain stunted physically, and deficient mentally. Successfully treated children may approach to normal, but the extent of this depends upon how early in life they are discovered to be cretinous.

(5) Treatment

Dry extract of thyroid, 1 to 3 grains daily, is required and must be used indefinitely; the dose is adjusted according to the clinical appearances.

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[References to other titles are given under Bones—Metabolic Dystrophies in the *Index Volume.*]

BONES—NEW GROWTHS

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1. BENIGN TUMOURS

69.] The classification in Table I covers both the common and uncommon types of simple tumour.

TABLE I

Osteoma—(osteochondroma)—cancellous or compact		Single Multiple—(diaphyseal aclasia)
Chondroma { ecchondroma enchondroma—(myxochondroma)—		{ Single—cyst Multiple—(dyschondroplasia)
Giant-celled tumour—(osteoclastoma)		
Haemangioma		
Subperiosteal lipoma		

(1) Bone and cartilage tumours

The tumours of this group present little difficulty in diagnosis as their clinical and radiographic features are sufficiently characteristic.

Osteochondroma and ecchondroma

(a) Single osteoma (osteochondroma) and solitary ecchondroma

These are found as painless, encapsulated tumours attached by a stalk or broad base to the end of a major long bone such as the femur, tibia or humerus (Fig. 128) or less commonly to a flat bone such as the pelvis, scapula or skull (Fig. 129). These tumours usually originate in early childhood and may remain small and inconspicuous for long periods. On occasion they grow

rapidly and may reach a considerable size (Fig. 130). In rare cases a chondroma may ultimately undergo malignant transformation, but it is important to realize that rapid growth and enormous size are not necessarily criteria of malignancy.



Fig. 128.—Male—age 17½ years—osteochondroma, upper end humerus.

(b) *Multiple osteochondromas*

These, on the other hand, are usually the outward manifestation of a skeletal growth disturbance (diaphyseal aclasia) in which the essential defect is the failure of normal tubulization in the metaphyseal ends of the long bones. Other prominent features of this condition, which may become noticeable only towards the period of adolescence, are stunting of growth and deformities of the forearm or leg bones (Figs. 131 and 132). Most of the tumours remain small, but one or more may grow and reach an inconvenient size.

The treatment of an osteochondroma or ecchondroma is to excise the tumour if it is causing inconvenience or exhibiting rapid growth. The stalk of these large tumours may extend deeply into the underlying bone and should be effectively eradicated to prevent recurrence.



Fig. 129.—Male—age 25 years—osteochondroma, ilium—left.

(c) *Enchondroma*

The favourite site is the miniature long bones of the hand or foot, and the tumour may take the form either of a solitary cyst containing myxochondromatous material usually involving the bones of the little finger (Fig. 133) or of widespread chondromatous change in the interior of a number of metacarpals and phalanges, accompanied by solid



FIG. 130.—Male—age 24 years—very large osteochondroma, pelvis.

growths budding out from the surface of the affected bones (Fig. 134). The latter type represents a growth disturbance which may be hereditary and familial. The solitary enchondroma cyst cannot be distinguished on clinical and radiographic evidence from a dystrophic cyst of a digital bone (Platt, 1930). Both types of cyst are liable to be discovered by chance when the thin shell has been fractured as a result of trivial violence. The enchondroma cyst in the active phase, in common with the dystrophic cyst, is best treated by curettage and packing the cavity with multiple bone grafts.

The solid tumours which, apart from disfigurement, may interfere with the free use of the fingers, should be effectively excised and the attenuated remains of the phalanges or metacarpals reconstructed by the insertion of strut bone grafts (Figs. 135, 136 and 137).

(2) Giant-celled tumours

The giant-celled tumour, or osteoclastoma (the myeloid sarcoma of the older writers), though essentially a benign neoplasm, as recognized in the middle of the 19th century by Paget, Nélaton and Virchow, is endowed with the potentiality of malignancy. In the long bones it is a comparatively uncommon tumour (Stewart, 1914). Conflicting views are held on the pathogenesis of this tumour; it is generally held to be a specific tumour of the fibrous framework of bone (Stewart, 1928). It has also been suggested that it is an aneurysmal expansion



FIG. 131.—Male—age 14 years—diaphyseal aclasia, showing failure of tubulization and small osteochondroma.

of bone (Codman, 1937). The typical osteoclastoma histology has long been familiar to surgical pathologists, but at least four histological variations have been distinguished (Ewing, 1928)—the myxoma type, the xanthoma type, the telangiectatic type and the cartilaginous type. The main features of the tumour, as contrasted with the closely related lesion, the dystrophic cyst, are set out in Table II.



Fig. 132.—Same case as in Fig. 131—forearm showing growth deformity.

Clinical types

Three clinical types of giant-celled tumour may be recognized (Platt, 1935a): (1) the indolent tumour—not a common type, (2) the aggressive and invasive tumour—perhaps the characteristic type (Fig. 138) and (3) the rare, but fully established, malignant type of tumour.

Table II

	Giant-celled Tumour	Solitary Bone Cyst
Age: years	20-35 (over 20)	5–15 (under 20)
Sex	More common in females	More common in males
Site of election	Femur—lower end Tibia—upper end Radius—lower end	Humerus—upper end Femur—trochanteric region Tibia—upper end
Site of origin	Epiphyseal	Metaphyseal
Clinical course	(Trauma) → pain → tumour Invasive and destructive	(Trauma) → fracture Spontaneous healing + +

Differential diagnosis

The giant-celled tumour has to be distinguished from a dystrophic cyst (typical or atypical), from an inflammatory lesion expanding the end of a long bone (Brodie's abscess), and from endosteal malignant tumours (secondary carcinoma deposits). Difficulties in differential diagnosis are rarely encountered.

Treatment

The rational treatment of the giant-celled tumour is based on the inherent invasive and destructive qualities of the average tumour. Prompt eradication by appropriate surgical procedures is the treatment of choice in all accessible tumours. Three types of operation are in common use: (1) curettage and cauterization, in early tumours (62 per cent of cures, Simmons, 1931); (2) excision, in tumours of the forearm bones or fibula (100 per cent of cures, Simmons, 1931); and (3) amputation, either as a primary measure,

Types of operation



FIG. 133.—Male—age 31 years—enchondroma, fifth metacarpal with spontaneous fracture.



FIG. 134.—Male—age 8 years—solid chondroma growths.



Fig. 135.—Female—age 13 years—enchondroma cyst in fifth metacarpal.



FIG. 136.—Same case as in Fig. 135—4 weeks after curettage of cyst and insertion of bone graft.

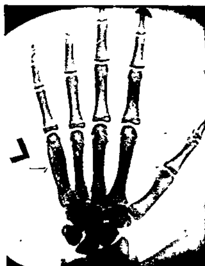


FIG. 137.—Same case as in Fig. 135—4 years later—showing cystic area completely replaced by new bone.



FIG. 138.—Male—age 26 years—giant-celled tumour upper end humerus—very aggressive type.

Irradiation

in tumours far advanced when first seen, and in proven malignant tumours, or as a secondary measure, after failure of more conservative operations (Fig. 139). Irradiation is best reserved for inaccessible tumours only, an attitude supported by the majority of surgeons who have devoted special attention to the giant-celled tumour problem.

(3) Rare tumours

(*a*) *The haemangioma*

This is usually found in the spine affecting a single vertebral body, or, more rarely, in the clavicle or flat bones (Paltrinieri, 1937). It is a slowly growing tumour, occurring generally in middle-aged individuals. When involving the lower thoracic spine it may be symptomless, and discovered by accident in skiagrams (Fig. 140); or, after a long period, may spread, and produce local pain and rigidity, root pains, or paraplegia, thus simulating Pott's disease or other forms of spinal tumour. The radiographic appearances are usually unmistakable.

The treatment for spinal haemangioma is rest, fixation, and irradiation for the relief of pain. In an accessible haemangioma, such as in the clavicle, resection should be carried out.

(*b*) *The subperiosteal lipoma*

This is a clinical curiosity, usually seen in the forearm in children. The clinical and radiographic signs are fairly characteristic and the tumour is easily eradicated (Fig. 141).

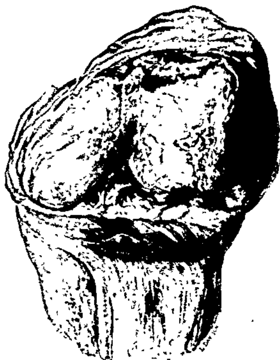


FIG. 139.—Male—aged 37 years—giant-celled tumour of lower end of femur—12 years' duration—showing impending invasion of the knee-joint.

2. MALIGNANT TUMOURS: PRIMARY

(1) Classification

The classification of primary malignant tumours is given in Table III.

TABLE III

BONE SARCOMA	Osteogenic sarcoma	Sclerosing; Osteolytic; Chondromyxosarcoma
	Ewing's tumour	
	Extraperiosteal sarcoma	
	Sarcoma in abnormal bones	Paget's disease; *Osteodystrophia fibrosa*; Osteochondroma
HAEMOPOIETIC TUMOURS IN BONE	Myeloma	Single; Multiple
	Reticulum cell sarcoma	
	Hodgkin's; lymphosarcoma; myelocytic myeloma; chloroma	
ADAMANTINOMA	Mandible	
	Other bones	

(2) General features

The primary malignant tumours of bone have two outstanding characteristics. In the first place they are comparatively uncommon, and in the second place they represent one of the most lethal forms of malignant disease. Their diagnosis rests on the evaluation of data obtained from a number of different sources—history, physical signs, and radiographic changes, reinforced, when required, by the naked eye and histological evidence of a biopsy. The great majority of malignant bone tumours run true to type, and the various composite patterns become increasingly familiar to those who are continuously engaged in the clinical study of this problem. A clear understanding of the significance of such factors as age period, sex incidence and site of origin of the tumour, whether epiphyseal, metaphyseal or shaft, is of primary importance. The main diagnostic features of the several types of primary malignant bone tumour may be conveniently illustrated in diagrammatic form (Figs. 142 and 143).

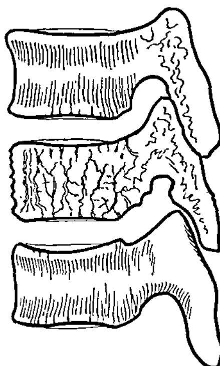


FIG. 140.—Haemangioma involving vertebral body in thoracic spine.

(3) Clinical features

Pain

In the history we find a characteristic sequence of pain as the earliest

Tumour Sarcoma

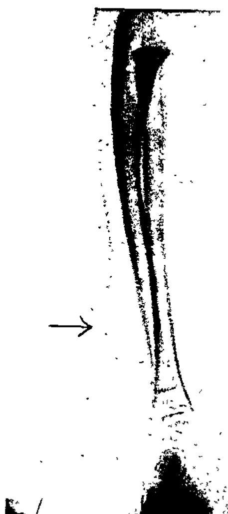


FIG 141.—Female—age 6 years—subperiosteal lipoma, ulna—lower third.

symptom, followed some time later by the appearance of a tumour which can be seen and felt. The tumour, in the *clinical* sense of the term, in the sarcoma group, is a clearly defined swelling, as one would expect from a well-encapsulated growth (Figs. 144 and 145). To the practised fingers, the contrast between a tumour and an inflammatory swelling of the bone and overlying soft tissues is most striking. This is true even of the Ewing's tumour, which in many respects may mimic osteomyelitis (Fig. 146).

Ewing's tumour

The earliest x-ray changes of localized bone destruction may be indeterminate, but when combined with the evidence of history and clinical signs may be suggestive or even conclusive. It should also be remembered that in the majority of sarcomas the main part of the tumour lies superficial to the bone and may be demonstrable as a soft-part shadow by appropriate radiographic technique.

(4) Biopsy

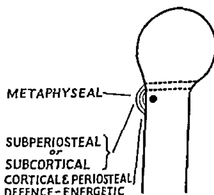
Biopsy

Biopsy as a diagnostic procedure has been the subject of much debate. The objections that it is both dangerous and imprecise have often been put forward, but the present-day majority opinion rejects this view. One of the advantages of biopsy to the surgeon familiar with the pathology of bone disease in the living body is the evidence afforded by the naked-eye appearance

FIG. 142.—Osteogenic sarcoma.

Age: 10–40. (Usually under 35.)
Sex: M. > F.
X-ray:
- Spindle swelling.
- Erosion of cortex.
- Radiating ossification.
- Extra-osseous tumour shadow.
  - Femur – – – Lower end.
  - Tibia – – – Upper end.
  - Humerus – – – Upper end.
  - Pelvis.

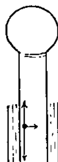
Trauma → Pain → Tumour
(Fracture 8%).



of the lesion. The material submitted for rapid histological examination in a biopsy should be a wedge of tissue so that deeper parts of the tumour are

available. More recently, the technique of aspiration biopsy has been practised with considerable success (Synder and Coley, B. L., 1945). I have found biopsy especially useful in the diagnosis of (1) atypical bone sarcomas such

*Fig. 143.—Ewing's sarcoma.
Endothelial myeloma.
Age: 10–15.
Sex: M. > F.
X-ray :
Thickened cortex.
Subperiosteal new bone, "onion layers".
Destructive changes.
Tibia.
Fibula.
Humerus.
Femur.
Flat bones.
Pain → tumour → febrile attacks.



as Ewing's tumour; (2) endosteal lesions such as atypical dystrophic cysts, giant-celled tumours and the rare, solitary myeloma; or solitary secondary malignant tumours in the long or accessible flat bones.



Fig. 144.—Male—age 15 years—osteogenic sarcoma; lower end left femur.



Fig. 145.—Same case as in Fig. 144.

Response to irradiation

A special diagnostic test in the Ewing's tumour is its response to irradiation. This may be of assistance in exceptional circumstances, but in my own view valuable time is liable to be wasted in awaiting the desired information.

(5) Prognosis and treatment

Bone sarcoma registry

Much of our statistical knowledge is derived from a study of material accumulated in the Bone Sarcoma Registry of the American College of

Surgeons. In 1934 the Registry included 74 five-year survivals out of 504 registered cases of osteogenic sarcoma, and 10 five-year survivals out of 126 cases of Ewing's tumour. All these long survivors had been treated by surgical measures, with or without irradiation and Coley's toxins. In the same year

Coley's toxins

W. B. Coley and B. L. Coley (1934) reported a personal series of 261 cases of tumours of the long bones, which included 35 five-year survivals in osteogenic sarcoma and 22 in Ewing's sarcoma. Of these, 47 had received toxin treatment and some of them irradiation in addition, but all accessible tumours had been treated by operation. In another series analysed by W. B. Coley (1933) of 160 cases of osteogenic sarcoma of the long bones treated by irradiation, when amputation had at first been refused by the patient, there were no five-year survivals unless the patient had subsequently consented to amputation. The conclusions drawn from these figures were that operation was the method of choice as soon as a diagnosis was established, and that in the considerable number of five-year cures then recorded in the United States of America, toxin treatment seemed to have played some part in the prolongation of life. Campbell (1935) in a series of 125 malignant tumours from the Registry and 14 personal cases, reported 14 cases of long survival, 10 osteogenic sarcomas, 3 Ewing's tumours and 1 extraperiosteal sarcoma. He was unable, however, to evaluate the effect of toxins and irradiation in the treatment of the Ewing's tumours.

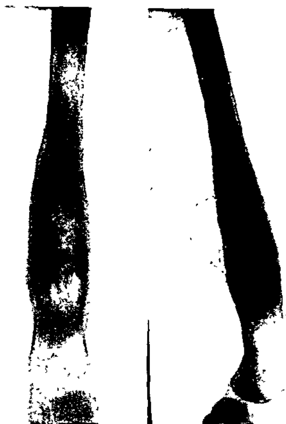


FIG. 146.—Male—age 17 years—Ewing's tumour, shaft of femur—lower third.

In 1939, the Bone Sarcoma Registry of the American College showed a large increase in the number of registered tumours of all types. There were then 101 recorded cases of five-year survivals in osteogenic sarcoma, and 14 in Ewing's tumour. Of the cases of osteogenic sarcoma 50 had been treated by surgical methods alone, and 50 by operation combined with irradiation, Coley's toxin, or a combination of these agents. Thirteen of the 14 cases of Ewing's tumour had also been treated by surgical methods. Bradley Coley (1938) reported 359 cases of osteogenic sarcoma from the Memorial Hospital treated by amputation, with irradiation combined with Coley's toxin in almost half the number. In this series there were 10·5 per cent of five-year survivals.

In the same year at the Mayo Clinic Meyerding (1938) reported a 24 per cent five-year survival rate in cases of osteogenic sarcoma following amputation, and a 9 per cent survival rate following irradiation alone. Simmons (1939) in a smaller series of 33 cases of osteogenic sarcoma, the majority treated by operation, recorded 11 five-year survivals. Simmons believed that pre-operative irradiation was a waste of time, and that biopsy as a preliminary to amputation is both useful and safe. With this view I am entirely in accord.

Results recorded 1941–1945

Preoccupation with the surgery of warfare has severely restricted the number of studies on bone-tumour problems during the period 1939–1945. In a recent valuable paper, Macdonald and Budd (1943) have analysed 118 five-year "cures" available up to that time in the Sarcoma Registry, using the new approved classification which distinguishes between osteogenic sarcoma proper (97 cases) and chondrosarcoma (21 cases). This analysis appears to show that the period of delay between the onset of symptoms and the initiation of treatment is greater in cured than in uncured cases. In this respect the authors, in common with B. L. Coley and Pool (1940), confirm Ferguson's findings (1940), but they do not agree with Ferguson's theory of the cycle of activity and regression in bone sarcoma as an explanation of this fact. Macdonald and Budd also find that a biopsy, or an even more extensive preliminary surgical intervention, does not militate against long survival; and that there is no statistical evidence for or against the value of irradiation as an ancillary curative agent.

(6) Personal findings

My own personal experience regarding survival rates is based on a survey of a series of 155 bone sarcomas of various types (1945, unpublished). In this series, up to date, there have been 23 five-year survivals, 16 cases of osteogenic sarcoma, and 7 cases of extraperiosteal sarcoma. There were no long survivors in the small group of Ewing's tumours. Of the 23 five-year survivals, 19 were treated by amputation or disarticulation (2 by hindquarter amputations), 3 by excision (in one of them followed by a disarticulation at a later stage), and 1 by irradiation alone (a sarcoma of the femur and pelvis but lacking histological proof). Coley's toxin was used in a small number of cases, but for various reasons it was impossible to apply this form of therapy in a systematic fashion.

It should be emphasized that many large primary malignant tumours of the pelvis are for a time operable by the method of hindquarter amputation. The outstanding contribution on this subject has been made by Gordon-Taylor (Gordon-Taylor and Wiles, 1935), who now has operated on 21 cases (personal communication, 1946). My own experience of this heroic procedure is confined to 6 cases, with 1 post-operative death 11 days later (Figs. 147 and 148).

(7) Summary

Osteogenic sarcoma

It can be said that although the outlook in osteogenic sarcoma is not as gloomy as we believed at one time, we still have no convincing data regarding the influence of histological or anatomical types of tumour in relation to survival periods. The spindle-cell type (fibrosarcoma) is believed with good reason to be the least malignant form, but the evidence regarding the degree of malignancy of the average chondrosarcoma is conflicting. All are agreed

Fibrosarcoma

Chondrosarcoma



FIG. 147.—Male—age 28 years—osteogenic sarcoma, ilium—right. Specimen of hindquarter amputation.



FIG. 148.—Same case as in Fig. 147—showing stump following hindquarter amputation.

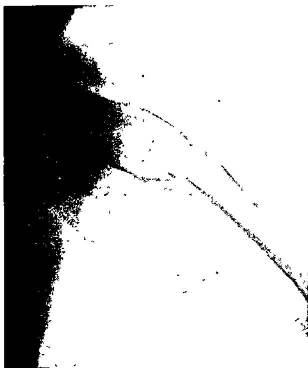


FIG 149 —Male—age 66 years—solitary plasmacytoma, humerus.



FIG. 150.—Female—age 24 years—extraperiosteal fibrosarcoma, femur.

Ewing's tumour

that the outlook in Ewing's tumour remains grave, but the reticulum-cell sarcoma recently differentiated from the Ewing group has been found to show a better prognosis (Parker and Jackson, 1939).

Haemopoietic tumours

Haemopoietic tumours in general are most lethal, but a solitary myeloma

(plasmacytoma) in a long bone may grow slowly for a long period, and offer the opportunity of temporary cure by resection or amputation (Fig. 149).

Extraperiosteal sarcomas

The group of extraperiosteal sarcomas contains tumours of varying degrees



Fig. 151.—Same case as in Fig. 150.



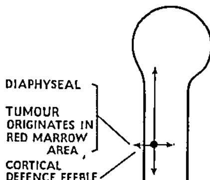
Fig. 152.—Same case as in Fig. 150—specimen. 19 years' survival after disarticulation.

of malignancy; some are relatively benign, and long survivals can be expected (Figs. 150, 151 and 152).

Adamantinoma

The adamantinoma, when involving the jaws, has long been familiar under the title of epithelial odontome as a slowly progressive lesion, relatively pain-

Fig. 153.—Solitary metastatic carcinoma.
Age : 40–60 + (Usually over 35)
Sex: M. = F.
X-ray:
Cystic expansion—trabeculated.
Destruction of cortex.
New bone formation.
Other bones: Punched-out areas.
Mottling.
Femur – – – – Upper $\frac{1}{3}$ shaft.
Humerus – – – – Upper $\frac{1}{4}$ shaft.
Pelvis.
Spine.
Pain → Fracture → Tumour
↓
(33 %).



less, which can be cured by excision. When appearing in a long bone—usually the tibia—this rare epithelial tumour is a clinical and pathological curiosity. At least 11 cases of adamantinoma of the long bones have been recorded



FIG. 154.—Male—age 49 years —a secondary hypernephroma in the upper end of femur. The skiagram shows the extent of the tumour 3 years from the first onset of symptoms. The tumour was removed by a disarticulation at the hip-joint in August 1934. At that time there was no clinical or radiographic evidence of the primary tumour. In February 1935 the presence of a primary tumour in the left kidney was suspected. On exposure of the kidney, a hypernephroma was discovered in the upper pole, and a successful nephrectomy carried out. There was no evidence of any other skeletal or visceral metastases.

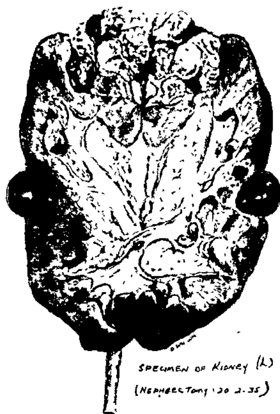


FIG. 155.—Same case as in Fig. 154—specimen of kidney with hypernephroma in the upper pole.

up to 1945. The tumour is a central expansile lesion affecting the shaft; the radiographic appearances are not specific and the diagnosis usually rests on biopsy findings. Resection of the affected area is the method of choice.

3. MALIGNANT TUMOURS: SECONDARY

(1) General features

Skeletal metastases are a familiar occurrence in the late stages of cancer of certain organs, most notably the breast, prostate, kidney, thyroid and bronchus. The cancer cells are distributed by the blood stream and deposited in the red marrow areas of the proximal parts of the long bones, and in the spine, ribs, skull and pelvis.

(2) Clinical features

Solitary metastatic tumours

A solitary metastatic tumour of a long bone (or occasionally of a flat bone) may be the first indication that the patient is suffering from malignant disease. In such cases the patient is often in good health and the primary tumour may remain hidden for a considerable period (Fig. 153). This picture is most likely to be seen in malignant adenoma of the thyroid and hypernephroma of the kidney. The solitary bone tumour may for a time simulate a primary tumour (Figs. 154 and 155), but at a later date other bony metastases may be discovered, or the primary tumour may be revealed after a careful search.

(3) Biopsy

Excision

Biopsy in such cases is of great value in establishing an early diagnosis. The radical removal of a solitary secondary tumour by excision or amputation is a justifiable procedure when the patient is suffering from intolerable pain, or when the affected limb has been rendered useless. On rare occasions the chance may be offered of prolonging life by eliminating both the primary tumour and the solitary secondary bony deposit (Platt, 1935b).

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[References to other titles are given under Bones—New Growths in the Index Volume. The subject of Bone Diseases is also dealt with in the *British Encyclopaedia of Medical Practice* (1936), Vol. 2, p. 553.]

BRACHIAL PLEXUS

(The subject of Cervical Rib is dealt with elsewhere in British Surgical Practice)

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Nuffield Professor of Orthopaedic Surgery, Oxford; Clinical Director, Wingfield-Morris Orthopaedic Hospital, Oxford

1. TRACTION LESIONS

70.] Brachial plexus injuries are remarkable in that most of them are due to traction, and it is therefore necessary to consider what happens in a nerve damaged as a result of sudden violence applied in its length.

(1) Pathology

Moderate stretching interrupts conductivity, without rupturing nerve fibres or causing any significant degeneration distal to the lesion. The resulting paralysis, neurapraxia (Seddon, 1943), has well-defined characteristics; it is predominantly motor—sometimes there may be no sensory disturbance whatever; the muscles do not degenerate and the reaction of degeneration never appears; recovery is rapid and complete.

Greater violence causes rupture of nerve fibres within their sheaths but no other significant disturbance (axonotmesis). Spontaneous recovery occurs, though it is slow since it depends upon regeneration of axons which have to travel a very long distance before making the connexions with end-organs upon

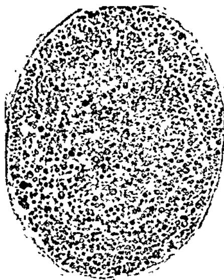


Fig. 156.—Transverse section of a nerve (stained Weigert) in which almost all the large, motor fibres—shown as black dots—are degenerate. Complete confirmation of the selective action of the traction force was obtained when the individual branches of the nerve were examined: only the motor nerves were degenerate. Rabbit's sciatic nerve: 50 days.

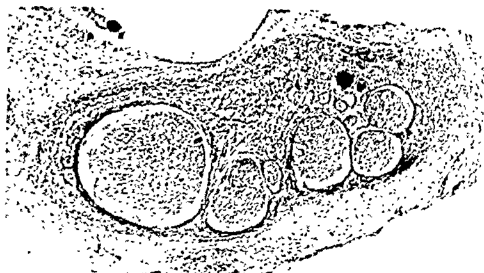


FIG. 157.—Transverse section of a nerve showing early epineural and perineural collagenization—the darkly staining zone round and between *the nerve bundles.* Rabbit's sciatic nerve: 9 days.



FIG. 158.—Lesion of C 5 and 6. Continuous line: anaesthesia. Dots: analgesia. Dark skin: normal sweating demonstrated by Guttmann's quinizarin method. In this case the zone of sensory loss extended well on to the *shoulder, which indicates involvement* of C 4.

which restoration of function depends. However, provided that the limb is properly treated the functional result will be very good *since there will have been no great* disturbance of the intraneural topography.

Not *infrequently one finds that* the paralysis—with evidence of degeneration—is purely or largely motor. *It* has been found experimentally (*Sanders* and Seddon, unpublished work) that the large motor fibres are more *susceptible to* damage by *traction* than the small sensory fibres (Fig. 156).

In *the next grade of severity,* rupture of the nerve fibres is accompanied by serious damage to the intraneural *blood-vessels* and connective tissue. Within a week or two a widespread interstitial change begins (Fig. *157); a* deposition of collagen (fibrosis) which strangles the nerve sheaths so that regeneration is either delayed and patchy or prevented altogether.

Great violence will rupture one or more of the trunks of the plexus, but the break is always accompanied by interstitial changes in both stumps, of the same kind that occurs in a severe lesion in continuity. *Rupture*



Fig. 159.—Lesion of C 5, 6 and 7.

Mixed lesions are by no means uncommon, the violence affecting different parts of the plexus in varying degree. All traction injuries are of considerable longitudinal extent, and signs of severe intraneural damage have been found over lengths of several centimetres. In most cases there is considerable disturbance of the surrounding tissues, especially the scalene muscles, and it has been supposed that the consequent fibrosis is responsible for the failure of regeneration in the nerve trunks. Hence, a plea has been made for early operation, though it is difficult to see what could be done in the absence of a nerve lesion so localized as to be amenable to surgical repair. The important point is that the significant damage is intraneural—and, so far as we know, irremediable.

(2) Clinical features

Just as there is every grade of intraneural damage, so there is every degree of involvement of the plexus; some of the more severe cases conform to one or the other of four easily recognizable types, the characteristics of which will be briefly summarized.

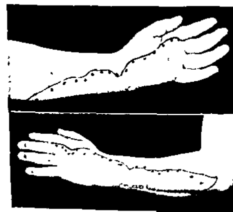
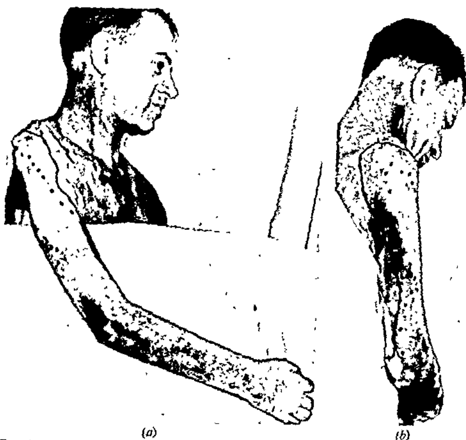


Fig. 160.—Lesion of C 8 and T 1.

The history, if available (the patient may have been rendered unconscious by the injury, in which case one can only surmise how the accident happened), often gives some clue to the sort of damage to be expected. In most cases there is a sudden depression of the shoulder, as when a man is thrown off a motor-cycle and lands on his shoulder. One would then expect the damage to be chiefly in C 5 and 6 with perhaps some involvement of C 7. Less frequently the shoulder is elevated, as when the subject is dragged along the ground by his arm or caught up in a parachute harness; in such a case the damage falls chiefly on C 8 and T 1. In the most severe injuries the



(*a*) (*b*)

FIG. 161.—(a) and (b). Lesion of C 5–T 1. Note characteristic *sparing of intercostohumeral zone in (b).*



FIG. 162.—Paralysis of cervical sympathetic in lesion involving C 8 and T 1. Loss of sweating and narrowing of palpebral fissure. The pupil (*not shown*) was also *smaller* on the affected side.

whole plexus is torn. Many patients presenting complete paralysis of the arm when first examined are later found to have only transient paralysis (neurapraxia) of one part of the plexus, which, clearing up within a few weeks, leaves the patient with an obvious degenerative lesion of the remainder. The zone of greatest damage is often supraclavicular; it may be high, in the region of the intervertebral foramina, or low, near the outer border of scalenus anterior. The most valuable pointers to the level of the supraclavicular lesion are the diaphragm, the rhomboids, serratus anterior and the cervical sympathetic; paralysis of any one of these indicates a high lesion. Infraclavicular lesions are manifest usually as interruptions of

separate trunks such as the axillary (circumflex) and musculo-cutaneous nerves.

(3) Signs

The pictures presented by the four main types of supraclavicular lesion may be summarized as follows (*see* tabular matter (for motor) and Figs. 158–162 (for sensory and sympathetic)).

A = lesion of C 5 and 6

B = what is usually regarded as a lesion of C 5, 6, and 7, though it may be more accurate to label it C 5 and 6 plus the posterior cord

C = lesion of C 8 and T 1

D = lesion of the whole plexus

	A	B		C	D
Diaphragm	(+)	(+)			(+)
Levator scapulae					(+)
Rhomboids	(+)	(+)			(+)
Supraspinatus	+	+			+
Infraspinatus	+	+			+
Serratus anterior	(+)	(+)			(+)
Pectoralis major, clavicular	(+)	(+)			+
„ „ sternal		(+)		(+)	+
Pectoralis minor					+
Deltoid	+	+			+
Teres major		+			+
Latissimus dorsi		+			+
Triceps		+			+
Biceps	+	+			+
Brachialis	+	+			+
Brachioradialis	+	+			+
Extensor carpi radialis longus	(+)	+			+
Extensor carpi radialis brevis		+			+
Extensor communis digitorum		+			+
Extensor minimi digiti		+			+
Extensor carpi ulnaris		+			+
Abductor pollicis longus		+	more or less involvement		+
Extensor pollicis longus		+			+
Extensor pollicis brevis		+			+
Extensor indicis		+			+
Pronator teres	(+)	+			+
Flexor carpi radialis	(+)	+			+
Flexor digitorum sublimis					+
Flexor pollicis longus			some weakness		+
Flexor digitorum profundus (lateral)					+
Intrinsics of thumb				+	+
Flexor carpi ulnaris		(+)		+	+
Flexor digitorum profundus (medial)				+	+
Ulnar intrinsics				+	+
Cervical sympathetic					

+ = almost always paralyse

(+) = sometimes paralysed



Fig. 161.—(a) and (b). Lesion of C 5–T 1. Note characteristic sparing of intercosto-humeral zone in (b).



Fig. 162.—Paralysis of cervical sympathetic in lesion involving C 8 and T 1. Loss of sweating and narrowing of palpebral fissure. The pupil (not shown) was also smaller on the affected side.

whole plexus is torn. Many patients presenting complete paralysis of the arm when first examined are later found to have only transient paralysis (neurapraxia) of one part of the plexus, which, clearing up within a few weeks, leaves the patient with an obvious degenerative lesion of the remainder. The zone of greatest damage is often supraclavicular; it may be high, in the region of the intervertebral foramina, or low, near the outer border of scalenus anterior. The most valuable pointers to the level of the supraclavicular lesion are the diaphragm, the rhomboids, serratus anterior and the cervical sympathetic; paralysis of any one of these indicates a high lesion. Infraclavicular lesions are manifest usually as interruptions of

(c) Relaxation of paralysed muscles by splinting, electrotherapy and re-education of muscles during recovery

These forms of treatment are no different from those required for other types of peripheral nerve injury and detailed description is, therefore, unnecessary. If the intrinsic muscles of the hand are paralysed they must be treated for a very long time, since even if regeneration proceeds at the normal rate re-innervation will not occur in much less than two years.

(6) Operative treatment

Since the prospect of recovery after the average traction lesion is not encouraging, the surgeon need have no hesitation in recommending reconstructive operations as soon as it is apparent that the paralysis has failed to clear up within reasonable time. If one regards one millimetre a day as about the normal rate of regeneration (Seddon, Medawar and Smith, 1943) and, assuming that the damage extends up to the transverse processes, allows twice the calculated time for recovery, and no significant improvement occurs, the paralysis must be regarded as permanent. In paralysis of C 5 and C 6 the aim is to restore flexion at the elbow and, if the patient desires it, though not everyone does, to stabilize the shoulder. The shoulder should be tackled first and arthrodesed by Watson-Jones's (1933) method, but the operation should not be done if thoraco-scapular control is poor. When the treatment of the shoulder has been completed, flexion of the elbow may be restored by Steindler's (1940) transposition upwards of the common flexor origin. A new operation, transplantation of the lower third of the pectoralis major into the biceps (Clark, 1946), offers a good prospect of restoration of flexion of the elbow in any case of brachial plexus injury in which the pectoral part of the pectoralis major is spared. The author has performed it in nine cases of brachial plexus injury, with satisfactory restoration of flexion and of some degree of supination in eight. In paralysis of C 5, 6 and 7 arthrodesis of the wrist by Smith-Petersen's (1940) method, which does not disturb either the flexor or the extensor tendons, may be combined with transplantation of acting wrist flexors into the extensors of the digits. Loss of flexion of the elbow can be controlled only by a splint, and some patients with paralysis of C 5, 6 and 7 will derive benefit from arthrodesis of the shoulder.

Paralysis of C 5 and 6

Paralysis of C 5, 6 and 7

The only operative treatment commonly called for in paralysis of C 8 and T1 is fixation of the first metacarpal in opposition, which compensates remarkably well for paralysis of the thenar muscles; a bone graft is inserted as a flying buttress between the first and second metacarpals.

Paralysis of C 8 and T 1

After complete brachial plexus palsy the patient is left with a completely useless limb, and the best way of dealing with it has not yet been determined. Two methods of treatment are now under trial. Amputation through the arm (which ought rarely to be done if the patient is still complaining of pain) may be combined with arthrodesis of the shoulder, provided thoraco-scapular control is good, the joint being fixed by a graft taken from the amputated limb (Perkins, personal communication). The best position is probably 15 degrees abduction and 10 degrees flexion, and it is then possible for the patient to control an artificial limb well enough to make the fitting of it worth while. The alternative, of which the writer has had no experience, is multiple

Swelling and tenderness may be found in the posterior triangle of the neck, and later, if C 5 and 6 are involved, a more or less localized swelling of the upper trunk of the plexus may be palpable. Pain in the whole of the upper limb or confined to the part chiefly affected is common in the early stages and may be severe. There may be associated fractures of the clavicle, shoulder or transverse processes. If the paralysis is extensive the limb will become more or less oedematous and stiffness, especially of the distal joints, will quickly follow unless prevented by the most energetic treatment.

Pain

(4) Prognosis

The non-degenerative lesions need not detain us since they will quickly be recognized by the normality of the electrical reactions persisting after the eighteenth day, and by recovery rarely delayed for longer than three or four weeks. A degenerative lesion confined to motor fibres, easily recognizable clinically, is likely to recover well, though not invariably so. The problem is how to distinguish between the other three types of lesion: (1) axonotmesis (simple axonal degeneration), (2) severe intraneural damage in continuity and (3) rupture of one or more of the trunks of the plexus. It may be said straight away that they are neurologically identical, since in every case there is complete peripheral degeneration in the distribution of the damaged nerves.

Identification of lesion

Exploration of the plexus is of value in distinguishing the predominant type of damage, but is hardly justifiable since, even if a complete tear is found, any attempt at surgical repair will be fruitless. Thus it is necessary to wait and see, and conservative treatment should be instituted forthwith. Any return of power or sensibility that occurs will almost certainly be incomplete—but none the less welcome. Useful recovery never occurs after a lesion involving the whole plexus.

Signs

Two signs are of value, in the negative sense of indicating a hopeless prognosis. If in a lesion involving C 5 and 6 a swelling can be felt on the nerve trunks in the posterior triangle of the neck, then it is certain that the damage to those roots is severe and that recovery will not occur. Similarly, in a lesion involving C 8 and T 1, paralysis of the cervical sympathetic is a bad sign.

(5) Treatment

(a) *Relief of pain*

Pain is due chiefly to the intraneural damage and the limb should be placed in such a position that the injured part of the plexus is not under tension. Analgesics may be required during the first ten days.

(b) *Prevention of oedema and stiffness*

The extent and severity of both are proportionate to the extent of the paralysis. They can be completely prevented by elevation of the limb, usually on an abduction splint, and by movements of all joints. At first these movements may have to be carried out twice or even three times a day. Pain and the presence of fractures may limit the extent to which this treatment can be enforced but in no circumstances should regular movements of the digits, active or passive, be omitted, and it is almost always possible to keep the wrist and elbow moving as well. In no other type of nerve injury is stiffness so prone to develop or the need for preventing it more urgent.

BRAIN—ABSCESS

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1. INTRODUCTION

71.] This chapter on brain abscess—a localized collection of pus within brain tissue—is written especially for the surgeon faced with the problem of diagnosing and treating this serious condition. Infections of the scalp, skull, subdural space, meninges or venous sinuses are covered elsewhere under their respective headings.

The author has utilized the experience gained during the past twenty years in operating on 105 consecutive patients with proven brain abscess. During the same period necropsy records on 47 consecutive patients, not operated upon, have been available for study. Most of this material (152 cases) passed through the Toronto General Hospital. The average yearly number of patients with brain abscess in a similar large general hospital, without a neurosurgical division or active surgical chest service, would probably be nearer one or two than eight.

2. SURGICAL PATHOLOGY

(1) Bacteriology

Pyogenic organisms

Practically all known pyogenic organisms produce abscesses of the brain. The infections arising from the ear or para-nasal sinuses are predominantly staphylococcal, streptococcal and pneumococcal. The abscesses secondary to chest infection are likely to contain a mixture of organisms, many of which are anaerobic. Gas-forming organisms are occasionally found enabling one accurately to locate the abscess by x-ray examination.

Our records do not indicate any special relationship between mortality rate and the organism; nor do we find any definite relationship between capsule formation and the type of organism. This is in keeping with Falconer's and his co-workers (1943) experimental work; he concluded that there was no deficiency in encapsulation with Gram-negative and anaerobic organisms.



FIG. 163.—Favourable single abscess adjacent to chronic ear disease; sudden death within a few hours of first stage of a two-stage operation under general anaesthesia.

(2) Cranial penetration

There are three well-known pathways by which infection may pass into the cranial cavity.

(a) By direct extension

Many brain abscesses secondary to middle ear and nasal sinus infection and trauma are examples of this—these are the favourable surgical groups because the brain abscess is usually single (Fig. 163).

(b) By preformed paths

These consist of arachnoid prolongations about the olfactory nerves. More important are the openings which lie in relation to the posterior cranial fossa, consisting of the internal acoustic meatus, aqueduct of the cochlea and vestibule and the hiatus subarcuatus. Certain cerebellar abscesses secondary to

middle ear infection are probably examples of spread of infection in pre-formed pathways. The brain has no lymphatic system, so spread of infection by this means is an anatomical impossibility.

(c) *By blood stream*

(i) *Arterial.*—This is the pathway when some focus elsewhere in the body causes a bacteraemia. For example, a brain abscess secondary to a skin infection or an endocarditis. On the whole these cases are an unfavourable group because of the serious general condition of the patient, plus the fact that the infection lodged in the brain is frequently multiple (Fig. 164).



Fig. 164.—Bacteraemia following severe burn (after early abscess formation); diffuse necrotic haemorrhagic infected lesions in cortex and subcortical white matter.

(ii) *Venous.*—A retrograde venous thrombophlebitis. This is the method of spread in certain cases in which the primary focus is in the middle ear or nasal sinus (Fig. 165). In contrast to the direct-extension abscesses these cases are unfavourable and more difficult to treat, first, because the brain abscess is frequently some distance from the primary focus and thus more difficult to locate, and secondly, this type of spread frequently results in multiple abscess formation. Brain abscess secondary to chest infection probably reaches the brain through the venous system (Fig. 166).

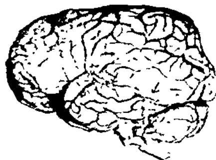


Fig. 165.—Acute otitis; the infected thrombosed tributary of the lateral sinus can be seen; the temporal-lobe abscesses were in the tissue drained by this vein.

(3) The abscess: favourable and unfavourable factors

When pus-producing organisms reach brain tissue by one of the above routes there is an immediate protective reaction on the part of the microglia. These cells mobilize and commence to remove by phagocytosis the necrotic brain cells and fibres. The vascular system in the brain reacts by proliferating and pouring out protective cells as it does elsewhere in any body tissue. *Microglial reaction*

At the end of three weeks a well-defined fibrous-tissue macroscopic capsule, enclosing pus, is formed. From the surgeon's standpoint the time at which a capsule may be expected to be *Abscess capsule*



FIG. 166.—History of chronic empyema; symptoms of brain abscess; no operation. There was a large chronic multiloculated abscess with a thick wall as well as two recent acute small abscesses.

well formed is important as, obviously, drainage before there is good localization is unsound.

A few abscesses resolve without drainage, others may become sterile and develop very thick walls over the course of months. For the most part, however, active surgical treatment is imperative a few weeks after the onset of the infection, despite active chemotherapy. A surgically untreated brain abscess will almost certainly kill the patient because of increased intracranial pressure, or rupture into the ventricle (Fig. 167), subarachnoid space (meningitis) or subdural space (subdural empyema) (Fig. 168).

The most favourable surgical cases are the single well-encapsulated abscesses



FIG. 167.—Rupture of abscess into the ventricle.

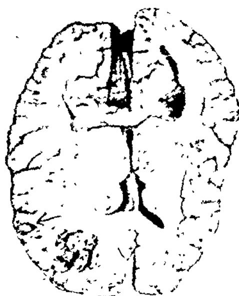


FIG. 168.—Acute pansinusitis; signs of brain abscess and meningitis; died shortly after radical drainage of frontal sinus. A small abscess had ruptured into the subarachnoid and subdural spaces.

adjacent to such primary foci of infection as the middle ear, nasal sinus and compound fractures of the skull.

In the group of 152 patients under discussion approximately one-third (57)

had multiple abscesses. Other unfavourable cases are patients moribund on admission from increased intracranial pressure, meningitis or subdural empyema, or some general serious systemic condition such as septicaemia. The surgeon may reasonably feel that in any large group of patients with brain abscess well over one-third are theoretically impossible to cure in the present state of our knowledge. *Multiple abscesses*

3. CLASSIFICATION OF BRAIN ABSCESS

The foci of infection causing brain abscess may be divided into five main groups (Table I).

TABLE I
GROUPING BASED ON FOCI OF INFECTION

Group	Primary Focus	Patients operated on	Necropsies: not operated on	Total
1	Ear { 1(A) Temp. Lobe 1(B) Cerebellum	36 10	4	50
2	Nasal sinuses	24	5	29
3	Chest	12	15	27
4	Various foci	13	21	34
5	Skull trauma	10	2	12
Total		105	47	152

The third column represents figures as they are encountered by the neurosurgeon in civil practice. The fifth column gives a better over-all picture as cases are added which for various reasons have not been operated upon. In the five groups, middle ear infection is the main focus of infection. Trauma is a causative factor in a small group. The remainder *are about equally divided between bacteraemia (various foci), nasal sinus and chest infection.*

Group 1.—Brain abscess secondary to ear infection (46 cases)

These abscesses are usually single and in 4 out of 5 patients are situated in the temporal lobe; in 1 out of 5 in the cerebellum.

Group 1 (A) *Abscess in the temporal lobe secondary to ear infection* (36 *cases*)

(*a*) *Symptomatology and diagnosis*

A composite history is somewhat as follows. An adult or child has a chronic or acute ear infection; this infection may have been treated conservatively or operated upon. There may be a few days of high fever and stiff neck indicating meningitis. The patient fails to make a satisfactory recovery in general health; the appetite is poor, the tongue is coated, the complexion is sallow; the patient prefers to stay in bed, becomes apathetic, mental acuity is mildly depressed, and he does not wish to be disturbed. There is persistent and severe headache, usually more marked in the frontal region on the side of the infected ear. During this period of two or three weeks the temperature swings from 97·5 to 99·5° F., and the pulse rate tends to be slow with occasional recordings of from 50 to 60. *History*

A brain abscess should now be suspected before the patient becomes so stuporous that a neurological examination cannot be made.

(b) *Special aspects of the neurological examination*

(i) *Ophthalmoscopic examination.*—The presence of choked discs plus ear infection practically establishes the diagnosis of brain abscess. The abscess will be on the side of the ear infection, and the chances are 4 to 1 that it is in the temporal lobe and not in the cerebellum. In Group 1 (A), of 36 patients 35 had choked discs at the time of operation, although an abscess was frequently suspected or diagnosed before the appearance of choking. When watching a patient one must appreciate that choked discs may develop rapidly and, when associated with increasing stupor, operation is urgently indicated.

Confrontation method

(ii) *Eye-field examination.*—Eye fields should be done by the confrontation method as fine perimetric examination is not possible in most cases. The test is definitely positive when the patient cannot see a moving finger on one or the other side. It is less positive but almost equally valuable if the patient has a tendency to look to one side and fix his gaze on one finger more than the other (attention field-defect).

Field defects

A field defect to the patient's right indicates a left temporal-lobe lesion, whereas a defect to the left indicates a right temporal-lobe lesion. Field defects were demonstrated in the majority of co-operative patients in Group 1 (A), at some stage in their illness. The absence of a field defect does not preclude abscess; its presence, however, determines localization in one or other temporal lobe.

(iii) *Pyramidal tract signs.*—A temporal-lobe abscess may interfere with the function of the pyramidal fibres streaming from the Rolandic area. One examines especially for some slight weakness of the lower face. There may be some demonstrable weakness of the arm and leg, with increased reflexes and an up-going toe. The abdominal reflex may be diminished. All or any of these signs when present are on the side opposite to the lesion, and can usually be demonstrated in co-operative patients in this group.

(iv) *Aphasia.*—Aphasia of varying degree (usually an inability to call people by their proper name, or to give the correct names of objects rapidly presented to the patient) was a helpful sign in the majority of the left temporal-lobe cases. Its absence, however, does not preclude abscess.

(v) *Lumbar puncture.*—Lumbar puncture should not be done unless it seems essential to confirm a clinical diagnosis of severe meningitis (in which case operation is not indicated unless the meningitis can first be controlled by chemotherapy). The author has seen a number of patients with brain abscess, who were good surgical risks become critical or hopeless problems within a few hours after a lumbar puncture. Rupture of the abscess or severe herniation through the tentorium may follow lumbar puncture. This is especially so if the patient is profoundly stuporous and has choking of the discs.

Results of lumbar puncture

(vi) *Miscellaneous signs.*—A few patients had a history of epileptic seizures, others had a sixth or third nerve palsy; several had nystagmus and hypotonia so that a cerebellar abscess was diagnosed, and the correct localization was only arrived at after negative exploration in the cerebellar region, or after a ventriculogram.

The history and findings as outlined above may be expected when the possibility of an abscess is suspected early, and one has the opportunity of following the course of the disease for a week or so. On the other hand, one may be called upon to deal with patients who have reached such a stuporous state

that neurological examination is practically limited to the establishment of two facts, namely, the presence of choked discs and a focus of infection.

Under such circumstances the surgeon does a ventriculogram before exploration; immediate operation is essential if the ventriculograms are positive, as a stuporous patient with a brain abscess will usually become critically ill within a few hours after a ventriculogram or a lumbar puncture. *Ventriculography*

Group 1 (B) *Cerebellar abscess secondary to ear infection* (10 *cases*)

(*a*) *Symptomatology and diagnosis*

The history and general condition of the patient is similar to that outlined in Group 1 (A) (temporal lobe). Headache and pain are more likely in the suboccipital region. Vomiting and dizziness may be outstanding features.

(*b*) *Special aspects of the neurological examination*

Nystagmus and incoordination were constant signs. These findings in the absence of a field defect localized the abscess in all cases. *Tests for incoordination*

(i) *Ophthalmoscopic examination.*—There was no suspicion of choking of the discs in 2 cases and only questionable choking occurred in 2 others. Choking of the discs was present in a higher percentage of the temporal-lobe cases, a finding contrary to what I would have expected.

(ii) *Miscellaneous findings.*—Involvement of some of the cranial nerves in the posterior fossa (third, fifth, sixth and seventh nerves) was occasionally seen.

Group 2.—Abscess secondary to nasal sinus infection (24 cases)

(*a*) *Symptomatology and diagnosis*

The history and general state of the patients were comparable to that outlined in Group 1 (A). In addition most of the patients had definite clinical evidence of frontal-sinus infection. Frequently one frontal sinus had been operated upon. Five patients had localized osteomyelitis adjacent to the frontal sinus on the side of the abscess. Four patients had severe spreading osteomyelitis of the frontal bone. A history of fits was obtained in 7 patients; usually these had lateralizing features. *Frontal-sinus infection*

(*b*) *Special features on neurological examination*

Sixteen patients had a lateralizing facial weakness and a few had a definite hemiparesis. Unilateral seizures and facial weakness were the definite lateralizing features in this group. *Pyramidal signs*

For diagnosis and lateralization ventriculograms were found necessary in a number of cases, and the practice should become routine. *Ventriculography*

Ophthalmoscopic examination.—Definite choking of the discs was found in 16 patients, and in 4 it was questionable. In 4 patients there was no choking.

Group 3.—Abscess secondary to chest infection (27 cases)

Operations were performed on 12 patients, and there were 15 additional patients who were not operated upon, the abscesses being found at necropsy. In only 25 per cent of these 27 cases was the brain abscess single. Almost without exception abscesses were not present in the body apart from the chest and brain. On the other hand, abscesses throughout the body were common in Group 4 secondary to widely scattered foci which produced a bacteraemia. This is the chief argument which is used against the infection being

transmitted through the arterial system to the brain in Group 3. Collis (1944) has discussed this problem, and concludes that the spread to the brain is probably by way of the venous system.

Symptomatology and diagnosis

The patient had a chest infection either within the lung or in the pleural cavity. Brain abscess is suspected when such a patient complains of headache and becomes apathetic. The clinical course is usually rapid, due to the multiplicity of the abscesses in the brain and the consequent widespread oedema and increased intracranial pressure. Rupture of these abscesses into the ventricle is common. Capsule formation is usually poor because the patients do not survive long enough.

Multiple abscesses

Group 4.—Abscess secondary to scattered foci in the body which have produced a bacteraemia (34 cases)

Operations were performed on 13 patients: 21 were not operated upon and the abscesses were found at necropsy. In only 25 per cent of these 34 patients was the brain abscess single. In this respect Group 4 is similar to Group 3.

Symptomatology and diagnosis

The general picture is quite similar to Group 3, although one more frequently sees a patient who runs a slower and more chronic course.

Group 5.—Abscess secondary to trauma (10 cases)

Symptomatology and diagnosis

These abscesses are usually single, and adjacent to an obvious compound fracture of the skull which has not been diagnosed or has been inadequately excised. The wound may or may not heal by first intention. The patient gradually shows the general signs of a brain abscess. Localizing features vary with the position of the abscess. In civil practice the group is small, whereas in war it represents the largest group.

Fracture of skull

4. DIFFERENTIAL DIAGNOSIS

(1) Meningitis

Presents the clinical picture of a restless or comatose patient flushed with high fever, marked rigidity of neck, and with milky cerebrospinal fluid.

(2) Subdural empyema

A history of nasal sinus disease, and often osteomyelitis of the frontal bone is usual, but it may occur in association with other foci of infection—epileptic seizures often lateralized, fever 102°–103° F., high white-cell count, moderate rigidity of the neck; often there is decided weakness of one leg as the important spread of pus is backwards along the falx with involvement of the upper Rolandic area. The diagnosis is established by exploratory burr holes in the suspected area.

Exploration of suspected area

(3) Brain tumour

Occasionally deep brain abscess develops without any very obvious focus of infection. The patient is afebrile, and a diagnosis of brain tumour is made largely because the possibility of brain abscess is not considered.

(4) Local encephalitis

Local encephalitis adjacent to a focus of infection may give all the signs of brain abscess. The diagnosis is only definitely established when there is a negative exploration for a brain abscess and the patient gets well. There is no certain way of making a diagnosis on clinical grounds alone; exploration is always indicated unless the patient is obviously getting better when he comes under observation.

5. SURGICAL TREATMENT

(1) *Timing of operation*

By preference one decides on operation when the history suggests intracranial trouble for a matter of weeks, that is at a time when good capsule formation may be expected. The surgeon's hand may be forced in the presence of a short history by serious stupor or coma; a patient in deep coma may not recover even though the abscess is drained. I am willing to postpone operation until some time in the future if the patient will respond actively in conversation. If, on the other hand, he has marked increase in headache, does not wish to be disturbed and is becoming stuporous, he becomes an emergency and should be operated upon immediately—not next morning.

A mastoid operation should not precede exploration for a brain abscess when the diagnosis is reasonably certain, and especially if drainage of the brain abscess appears to be an urgent matter. The mastoid operation can be partially done when the abscess is located and drained, and completed in detail when the abscess is cured. In patients who are in good shape and who are only suspected of having a brain abscess a mastoid operation should precede intracranial exploration. In a number of these patients extradural pus will be found, and intracranial symptoms will rapidly clear up. These patients require careful watching for several weeks before discharge from hospital; some of them will develop brain abscess. An intracranial exploration should not be carried out through a contaminated field unless one is certain that an abscess will be located, because organisms can in this way be implanted in the brain. *Mastoid operation*

(2) Anaesthetic

Local anaesthesia by infiltration of the operative site with 1 per cent procaine (Novocain) is preferable in a co-operative patient. Local anaesthesia gives the surgeon a choice of a one-stage or a two-stage operation; in the latter the abscess may be uncovered or located, and drained at a later date when adhesions have formed between the brain and the dura. It is dangerous to plan a two-stage operation with general anaesthesia as the patient may not waken after a general anaesthetic when the abscess has been left undrained. General ether anaesthesia administered through an intratracheal tube, so that a free airway is well established at all times, is preferable in the stuporous non-co-operative patient. *Local anaesthesia* *General anaesthesia*

(3) Operation

The whole head should be shaved as there is no certainty that the suspected site only will be explored. Furthermore, post-operative dressings are easier when all hair has been removed. Certain special equipment is helpful: (1) suction with variable sizes of metal or glass suction tips, (2) an endotherm *Special equipment*

machine for controlling bleeding in the brain, (3) a good spot light or head light, (4) two narrow, flexible brain retractors, (5) a nasal speculum with blades 2 inches in length, (6) skull burrs, (7) a brain needle, (8) special brain-abscess drainage tubes.

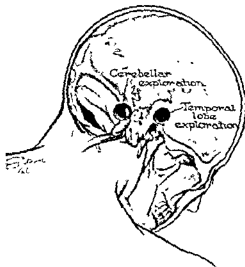


FIG. 169.—The prone position, with the head turned to one side, gives adequate exposure for temporal lobe and cerebellar exploration.

Position of patient

When the abscess is secondary to ear infection, the patient is placed on the table in the prone position with one shoulder supported by a sand-bag (Fig. 169). In this position the anaesthetist has good access to the patient; a restless patient can be controlled more easily; the surgeon can operate on either the infratentorial or supratentorial region. When infratentorial exploration is not anticipated a semi-sitting position with the head in a crotch head-rest gives good access to all supratentorial regions (Fig. 170).

(4) Temporal lobe abscess

A burr hole is made over the suspected area through a clean field because the exploration may be negative. A small opening for the brain needle is made in the dura. One anticipates being able to palpate the asbcess capsule just beneath the surface with a blunt-pointed brain needle. If an abscess capsule is palpated the burr hole is usually enlarged towards the mastoid process, and if a mastoid operation has not been done these cells may be rapidly opened to provide drainage of this infected area. The final dural exposure is usually from $\frac{3}{4}$ inch to 1 inch in diameter. The dura is opened in a stellate fashion. The immediate underlying brain is sucked out, bleeding controlled by endothermy and the abscess cavity brought into view. An opening is made into the cavity, and the margins of the capsule are grasped in fine tooth forceps and held up to prevent the brain falling away from the dura, as it occasionally does. At the same time the sucker is introduced into the cavity and pus is sucked out. A nasal speculum may now be introduced, and the cavity

Dural exposure

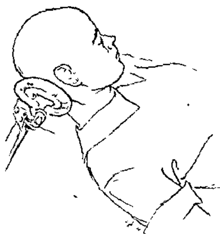
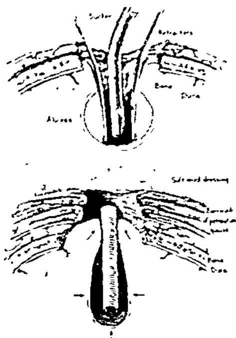


FIG. 170.—Semi-sitting position with the head supported by a crotch head-rest, gives adequate exposure for all supratentorial regions including a ventriculogram.

thoroughly sucked out and inspected for secondary sinuses leading to pockets. A tube, $\frac{1}{4}$ inch to $\frac{1}{2}$ inch in diameter and without side openings, is placed to the bottom of the cavity and cut off flush with the dura. The scalp margins are sutured back to control haemorrhage and give direct access to the tube. A dressing of gauze soaked in penicillin or a sulphonamide cream is applied, and held in place with a carefully applied flannel bandage. The first dressing is usually done 3 or 4 days later when the tube may be rotated and possibly shortened slightly. Subsequent dressings are done every few days, and the tube gradually shortened over a period of a few weeks. If the tube is pushed out by the patient disturbing the dressing, it can usually be accurately replaced by doing a lumbar puncture, and draining sufficient cerebrospinal fluid to lessen tension, so that the sinus and abscess cavity open up and can again be thoroughly inspected.

Dressings



Chemotherapy is continued for at least a week after operation.

Chemotherapy

Cerebral hernia is not troublesome when the dural opening is not much larger than the drainage tube; drainage should be at right angles and not oblique (Fig. 171). Any slight herniation will gradually subside over a period of weeks after the drainage tube is finally discontinued. Before the era of chemotherapy a two-stage operation under local anaesthesia was desirable to prevent meningitis developing at the site of drainage. Today a one-stage operation, with tube drainage through a small dural opening directly over the point where the abscess is close to the surface, is the procedure of choice. For a deeper abscess this procedure is not satisfactory, because there is great difficulty in getting a tube successfully placed in the abscess when working through a relatively small dural opening.

One-stage operation

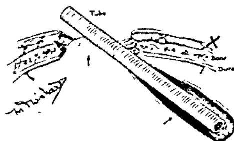


Fig. 171.—Illustrating simple tube drainage for a superficial abscess. Oblique drainage is undesirable; herniation may be much more difficult to control and there is a tendency for the abscess to pocket; X = correct position for bone opening.

(5) Deep abscess

For the deeper abscesses the following procedures are advocated.

(a) Penicillin injection

The abscess may be gently aspirated through the brain needle and penicillin injected into the cavity—the wound may be closed, and the procedure repeated if and when symptoms return or persist. In our experience a single tapping has never been successful—many such cases are, however, reported.

(b) Thorotrast injection

The procedure of injecting Thorotrast (Kahn, 1939) into the cavity is valuable, as repeated x-ray examinations then give visual information regarding progress and location.

Plastic tubes

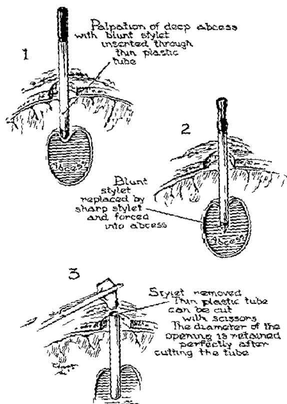


FIG. 172.—Illustrates a simple method of introducing a special thin plastic tube into a deep brain abscess.

(c) Drainage

The brain needle, or preferably one of the special plastic brain-abscess drainage tubes, may be left in place (Fig. 172). These thin plastic tubes will not stand boiling or autoclaving, or cold sterilization with Bard-Parker solution; they may be sterilized by soaking in any strength of perchloride of mercury solution. The tubes may be obtained from J. F. Hartz and Co., Toronto. Careful aspirations and injections of penicillin can then be carried out every few days. This procedure appeals to me more than repeated tappings as there is danger of making new infected needle tracks or even of not being able again to locate a deep small abscess. When using this type of drainage, or any other for that matter, it is important to prevent contamination of the end of the tube by other organisms, especially *Bacillus proteus* which is highly resistant to chemotherapy.

(d) Alternative method of operation

King's method

Another method, advocated by King (1936) and successful in his hands, is to make a larger dural opening, remove brain tissue and open up the abscess widely. The floor of the abscess is gradually herniated out. The hernia is kept under control by repeated lumbar punctures and expert care in dressing. The author has had little experience with this method, feeling that there would often be too much damage to essential brain areas. It might easily be the only feasible method in certain traumatic cases.

(e) Further procedure

After repeated tapping the capsule may become quite thick and prevent further tapping; or the patient may remain well for a period and then again

show evidence of pressure. Complete removal of the abscess cavity, using a brain-tumour removal technique, may then be the procedure of choice. Occasionally, after tube drainage of a fairly superficial abscess there is re-formation of pus, often multi-loculated; complete removal or unroofing of the whole area as advocated by King is the only feasible method of eradicating the lesion. *Removal of abscess cavity*

(f) *Summary*

In brief the author advocates a one-stage tube drainage for the superficial abscesses. For the deeper abscess the special plastic brain-abscess tubes, with repeated instillations of penicillin along with Thorotrast, so that the abscess may be visualized, is the method of choice. These tubes are designed for simple introduction into a deep abscess (Fig. 172). If the abscess re-forms it should be removed *in toto* using a brain-tumour technique.

The techniques described are applicable to brain abscess wherever located.

(6) Frontal lobe abscess

In the frontal cases the abscess may be superficial or deep. The frontal sinus should be obliterated by removing the posterior wall, if such a procedure would appear to provide more superficial and direct drainage. The abscess is first palpated through a burr hole in a clear field. The principle of direct drainage at a point where the abscess is closest to the surface is sound. The author has frequently closed the first burr hole after locating an abscess, and drained through a second bone-opening made at a point where the abscess is closer to the surface. Oblique drainage of an abscess favours pocketing and recurrence, and the formation of troublesome or disastrous herniation (Fig. 171). *Obliteration of frontal sinus*

(7) Abscess associated with compound fracture

In abscesses secondary to compound fractures of the vault no special technique is required as these abscesses are usually superficial, with well-formed adhesions between dura and arachnoid. It is important to remove any depressed fragment of bone or readily accessible foreign body. The most important factor is the prevention of abscess-formation by adequate treatment of the primary injury.

6. CEREBRAL FUNGUS

For an account of the management of this complication the reader is referred to the article on Brain Fungus.

7. SUMMARY

Table II shows the over-all mortality rate. Table III shows the incidence of epilepsy in the whole group.

In conclusion, one can state that almost one-third of an unselected group of patients will have multiple abscess formation or other severe complicating factors—only a few of these will be saved. Chemotherapy will in the future bring the operative mortality rate closer to 30 per cent than 53·4 per cent as in this series. Spread of infection at the drainage-site before the era of chemotherapy has been one of the major factors causing death. Most patients who

TABLE II
TOTAL OPERATIVE MORTALITY

GROUP	PRIMARY FOCUS	PATIENTS OPERATED ON	ALIVE	DEAD	MORTALITY %
1	Ear { 1(A)Temp. Lobe	36	19	17	47·2
	1(B)Cerebellum	10	5	5	50
2	Nasal sinuses	24	13	11	45·8
3	Chest	12	1	11	91·6
4	Various foci	13	4	9	69·2
5	Skull trauma	10	7	3	30
Total		105	49	56	53·4

TABLE III
PATIENTS WITH EPILEPSY POST-OPERATIVELY

GROUP	PRIMARY FOCUS	ALIVE	EPILEPSY	% EPILEPSY
1	Middle ear { 1(A)	19	1	5·3
	1(B)	5	0	0
2	Nasal sinuses	13	5	38·4
3	Chest infection	1	0	0
4	Various foci	4	4	100
5	Skull trauma	7	5	71·4
Total		49	15	30 6

recover from a brain abscess become useful citizens although almost one-third will suffer from epileptic seizures of varying degree and frequency.

The author is indebted to Professor Eric A. Linell for access to his neuropathological files and for the privilege of using a number of illustrations from his files.

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[References to other titles are given under Brain—Abscess in the Index Volume. The subject of Brain Abscess is also dealt with in the *British Encyclopaedia of Medical Practice* (1936), Vol. 2, p. 597.]

BRAIN—CONGENITAL DEFECTS

By G. F. ROWBOTHAM, B.Sc., F.R.C.S.
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1. DEFINITION

72.] The central nervous system is developed from a cylinder of ectodermal cells known as the primitive neural canal. The skull and dura mater arise from the mesodermal element which surrounds this canal. The scalp is ectodermal in origin. Developmental errors of the scalp and skull therefore have to be considered with those of the brain.

Many congenital anomalies of the head are incompatible with life or with a reasonable form of existence, and of these anencephaly, cyclops and arhinencephaly may be mentioned.

Anencephaly is a condition in which the whole of the vault of the head is absent. Cyclops is a severe anomaly in which there is total fusion of the cerebral hemispheres; the orbits are also fused and may contain 1 or 2 eyes; the nose is absent. Arhinencephaly is a milder degree of cyclops deformity and consists essentially of the absence of the highest centres of the brain.

The following is an account of those anomalies of the head with which the surgeon is liable to be confronted.

2. DEFECTS OF THE SCALP

Fissures and areas of skin covered by parchment-like tissue sometimes occur. The hair may grow in peculiar patterns and in different colours.

Arteriovenous haemangioma (cirsoid aneurysm) (Fig. 173)

This is the most important developmental anomaly of the scalp. It is not *Pathology* a form of capillary or cavernous angioma but is essentially a progressive

pathological dilatation of veins and arteries resulting from a congenital communication between an artery and a vein, which allows the full force of the arterial blood stream to act on a thin-walled vein without the protective barrier of the capillary bed.

Symptoms and signs

Often this condition does not begin to declare itself until puberty or the early twenties. The swelling may first be noticed on combing the hair; pain is rarely felt. Gross disfigurement occurs when the vessels of the face distend, but spontaneous rupture of the vessels is rare. The signs are unmistakable; the



FIG. 173.—This photograph shows the bulge of an arteriovenous aneurysm on the vertex of the head. From it large vessels can be seen radiating extensively over the left side of the scalp.

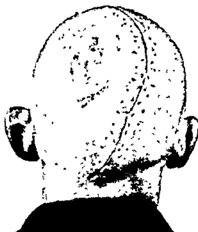


FIG. 174.—For the adequate removal of an arteriovenous aneurysm of the scalp a wide surgical exposure is necessary. Imperfect surgical removal means recurrence.

swelling on the scalp pulsates and there is a forcible thrill on palpation and a loud bruit on auscultation.

Treatment

Treatment is not an easy problem because of the difficulty in controlling bleeding and because the vessels are embedded in the dense fibrous tissue of the scalp, superficial to the galea, and do not dissect or strip out readily. The method I have found most valuable for removal is as follows. The entering vessels, whether arterial or venous, are ligated at a reasonable distance from the main tumour, through separate small incisions; a skin flap is then turned down containing the main part or, if possible, the whole of the aneurysm, the incision being made and the artery forceps applied under careful digital pressure. The vessels are ligated or diathermized from the pericranial side of the flap and then excised. If radical removal is not performed the tumour almost certainly will recur. (Fig. 174.)

3. DEFECTS OF THE SKULL

(1) Craniolacunia

This condition is characterized by an abnormal ossification of the bones of the vault of the skull. Radiologically, the skull shows a mosaic pattern of thin poorly-calcified areas of bone enclosed by thick bars or ridges. (*See* Bones—Errors of Development and Growth [Lacuna Skull], p. 266.)

(2) Cranium bifidum

This term implies that there is a deficiency in the bones of the skull and that one of the elements of the intracranial cavity has herniated through the defect. Usually the defects are either in the occipital region or at the root of the nose. If the meninges only are herniated, the condition is known as a cranio-meningocele (Fig. 175). If brain substance is included, the condition is known as an encephalo-meningocele. Both conditions are often associated with deformities of the brain.



FIG. 175.—An occipital meningocele is frequently associated with a maldevelopment of the cerebellum.

Treatment

Treatment consists in excision of the sac with plastic repair of the calvarial defect.

(3) Craniostenosis

Implied by this term is a premature closure of a cranial suture, due to a fault in ossification, the nature of the resulting deformity of the vault depending upon which suture or sutures are affected (Fig. 176). When the sagittal and coronal sutures unite prematurely, the vault continues to grow upwards but not antero-posteriorly or laterally, with the result that the vault becomes shaped like a cone. This condition is known as oxycephaly or steeple head (Fig. 177). (*See* Bones—Errors of Development and Growth [Acrocephaly], p. 266.) Scaphocephaly means a boat-shaped head (Fig. 178) and plagiocephaly an obliquely-flattened head.

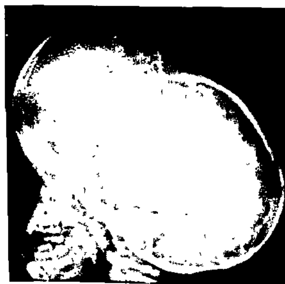


FIG. 176.—In craniostenosis faults in ossifications of the sutures lead to asymmetry of the skull.

Treatment

Treatment consists in the surgical removal of a strip of bone, excised in such a way that the skull is allowed to distend as the brain enlarges.

(4) Basilar invagination (platybasia)

Pathology

This condition is a deformity occurring at the cranio-spinal junction. The foramen magnum is thrust upwards and invaginates into the posterior

Symptoms and signs

fossa. Usually the atlas is fused to the skull and the axis is rudimentary. The neck is short and the movements of the head are restricted. Pressure upon the medulla and upon the upper part of the spinal cord, and blockage of the cerebrospinal fluid pathways, may simulate a posterior cranial fossa tumour.

Treatment

Treatment consists in suboccipital decompression and laminectomy of the atlas and axis vertebrae.

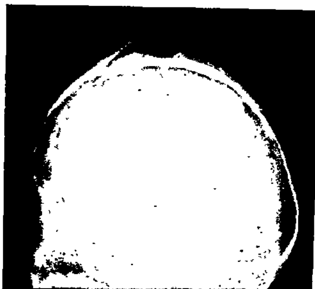


FIG. 177.—A skull may grow in the form of a turret. *The skiagram shows the steeple head of oxycephaly.*

4. DEFECTS OF THE BRAIN

The varieties of malformation of the central nervous system are manifold, and the brain tissue proper, the cerebrospinal fluid pathways or the vascular system either singly or in any combination may be affected.

(1) The brain tissue proper

(*a*) *Microcephaly*

Here the whole of the brain is grossly under-developed, the clinical picture being that of a mentally defective child with a tiny skull and a slanting forehead.

(*b*) *Faults in the gyri*

(i) *Lissencephaly*.—This is the name given to the condition when the gyri are fused into a mass so that the hemispheral surfaces appear smooth.

(ii) *Pachygyria*.—In this condition the cerebral convolutions are abnormally broad.

(iii) *Microgyria*.—There are, in this condition, sunken pits on the surface of the cerebral hemispheres, lined by abnormally small gyri which are largely composed of glial tissue. The clinical picture in these states is very variable; there may be no symptoms or symptoms may range from occasional epileptic attacks to mental defectiveness.



FIG. 178.—Scaphocephaly is a head with a keel. The child in this case was mentally defective.

(*c*) *Porencephaly* (Fig. 179)

This term implies that there is a hole in the brain. In the extreme type a channel connects the ventricles with the surface spaces; *often all that exists*

is a diverticulum connected either with the ventricles or with the surface spaces alone. The clinical picture is typically that of mental defectiveness and epilepsy. The minor forms, however, may be symptomless.



FIG. 179.—Porencephaly or hole in the brain can be demonstrated during life by encephalography.

(*d*) *Faults in myelinization*

Mental defectiveness in infants is, in my opinion, more commonly due to congenital defects in the brain and, in particular, to faulty myelinization than to birth injuries or to prenatal or post-natal infections. Moreover, I believe, such faults account for many of those cases which are clinically grouped as Little's diplegia or infantile hemiplegia.

(*e*) *Agenesis*

Complete non-development of one or more anatomical units of the brain characterizes this condition.

(i) *Of the cerebellum.*—The photograph shows the brain of a young man who was killed on the road at the age of 20 and who had never shown signs of lack of balance or muscle co-ordination, although the left lobe of the cerebellum had never developed (Fig. 180). On the other hand, when the vermis of the cerebellum fails to develop gross ataxia and lack of balance are usual.

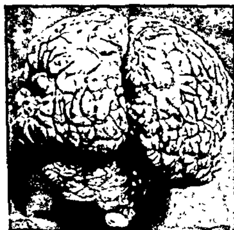


FIG. 180.—A whole lobe of the cerebellum can fail completely to develop. In this case the maldevelopment did not lead to ataxia or to faults in balance. The patient died as the result of a head injury.

(ii) *Of the corpus callosum.*—Faults in the development of the corpus callosum may be partial or complete. They may be demonstrated by air studies, when a cyst filled with air is shown to occupy the median line in place of the septum pellucidum. The clinical picture is that of feeblemindedness and epilepsy.

(*f*) *Arnold-Chiari syndrome*

The Arnold-Chiari malformation is characterized by displacement of the lower part of the medulla and cerebellar lobes into the spinal canal. Symptoms are caused partly by impairment of the cerebrospinal fluid circulation, resulting in hydrocephalus—partly by pressure on the upper part

of the spinal cord or medulla, and partly by the stretching of the upper cervical nerves and the jugular group of cranial nerves.

Diagnosis usually depends upon the presence of an accompanying spinal meningocele. When there is no meningocele the picture may closely resemble that typical of a tumour in the posterior cranial fossa.

Treatment

Treatment consists in suboccipital decompression and laminectomy of the upper 2 cervical vertebrae.

(2) Cerebrospinal fluid pathways

Faults in the development of the cerebrospinal fluid pathways may occur anywhere from the arachnoid villi to the foramina of Monro. The villi, which are the absorptive mechanism of the system, may be completely absent or isolated by failure of the arachnoidal membrane to reach and envelop them. The foramina of Magendie and Luschka may be absent; the aqueduct of Sylvius may be stenosed and one or both of the foramina of Monro may be occluded by a membranous fold. Faults in cerebrospinal fluid drainage result in hydrocephalus, of either the external or internal type, according to the site of blockage.

(3) Vascular anomalies

(a) Arteriovenous haemangiomas or cirsoid aneurysms of the cortex of the brain

The aetiology and pathology of arteriovenous haemangiomas of the cortex are identical with those of the scalp. In fact, on occasion both the brain and the scalp may be affected, communications between the surface and deep vessels occurring through channels in the bone. Typically, the aneurysms appear as worm-like collections of thin-walled dilated vessels on the surface of the brain. They may remain symptomless for life or may at any age set up a progressive cerebral atrophy and cause epileptic seizures. They may or may not be associated with enlargement of the diploic veins of the skull and radiography may show parallel lines of calcification. There is no bruit and no thrill unless the condition has extended to the tissues of the scalp. Diagnosis is made by operative exposure or by angiography.

Treatment

Treatment is given by deep x-ray therapy, excision rarely being feasible.

(b) Saccular aneurysms

These aneurysms occur chiefly on the large trunks of the vessels of the circle of Willis and result either from a defect in the mesodermal coat of an artery or from the persistence of the primitive bud of an embryological vessel, which normally shrivels and disappears. According to their position in relation to the anterior clinoid process, saccular aneurysms may be classified as supraclinoid or subclinoid.

(i) *Subclinoid aneurysms.*—Although rupture of aneurysms in this position is common, diffuse bleeding into the intracranial cavity is rare because the coats of the aneurysms are strengthened by the walls of the cavernous sinus. Such aneurysms are a cause of severe and persistent headaches and of pains in the face. Sudden enlargements, due, no doubt, to local rupture, are usual, with the result that nearby structures—particularly the ocular nerves—are stretched, causing sudden ocular palsies, especially of the third cranial nerve. Diagnosis can be definitely established by angiography.

Treatment consists in ligation of the internal carotid artery in the neck. Digital compression of the artery on the affected side (through the skin) for increasing periods for several weeks preceding contemplated ligation will ensure as far as possible that the cross circulation between the two sides of the circle of Willis is sufficient to prevent hemiplegia when actual ligation takes place. *Ligation of internal carotid artery*

(ii) *Supraclinoid aneurysms.*—These are usually symptomless until a severe cerebral catastrophe occurs in the nature of a sudden and severe subarachnoid haemorrhage. Typically, a previously healthy young or middle-aged person is struck with a sudden and severe pain in the head which rapidly radiates into the neck and may reach as far as the fingers and toes. Consciousness may be impaired and cranial nerve and other palsies may or may not occur.

Treatment is usually conservative and consists in keeping the patient quietly in bed until the ruptured vessel has soundly healed. When medical treatment fails, or after recurrent haemorrhages, it is sometimes necessary to expose the aneurysm and to remove it, to destroy it by coagulation or to strengthen its walls with muscle grafts. *Treatment*

(iii) *Cavernous haemangiomas in the new-born.*—This is a rare but very dangerous condition if its true nature is not recognized. A new-born infant may be perfectly well in every way apart from a local swelling on the head which is very suggestive of a simple cephalhaematoma. In the swelling there may be no thrill, no bruit and possibly no discoloration of the skin. X-ray examination shows that the bone is thinned and bulged and occasionally absent altogether.

Diagnosis can be confirmed by aspiration, when pure blood is withdrawn into the syringe. In all cases of suspected cephalhaematoma, aspiration with a fine-bore needle should be made. Incision into a cavernous haemangioma with a scalpel will almost certainly be fatal.

[References to other titles are given under Brain—Congenital Defects in the Index Volume.]

BRAIN—FUNGUS

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1. DEFINITION

73.] A brain fungus is a protrusion of brain tissue through a defect in its covering scalp, skull and meninges.

2. AETIOLOGY

The condition occurs as a complication of head wounds. These wounds usually result from injury and are especially common in warfare since missiles so frequently penetrate the brain in addition to destroying an area of its coverings. In the past, brain fungus was seen not infrequently in the operative wounds through which brain tumours had been approached. With the modern two-layered closure of the scalp this complication of such operations is rare, even in the presence of high intracranial pressure.

3. ANATOMY AND PHYSIOLOGY

In normal circumstances the cranial cavity accommodates its contents at low pressure. In certain postures the intracranial pressure will be a little above that of the atmosphere, and in other postures it will be subatmospheric—as is indicated by the deep depression of scalp into a cranial defect which may be seen in old head wounds. In most postures it will therefore be found that there is little tendency for the brain to protrude through a defect in its coverings. Should such a defect be associated with raised intracranial pressure, however, the tendency for protrusion to occur will be great. After a penetrating head wound the pressure within the skull may be increased as a result of the brain injury itself or of some infective complication, and in these circumstances there is an obvious risk of protrusion of cerebral tissue occurring, with the formation of a cerebral fungus. There is another type of cerebral fungus which is not due to intracranial hypertension since no cause for such hypertension can be found and the cerebrospinal fluid pressure can be shown to be within normal limits. Its cause is not obvious, and several hypotheses have been put forward (Magnant, 1927). It cannot be accepted that fungation in these cases is due to the absence of cerebral coverings or to the pulsation in the cerebral vessels. The suggestion that a cerebral fungus represents brain tissue strangulated by the margins of the cranial defect (Leriche 1916) is unsatisfactory, since it is the dural opening which surrounds the neck

With intracranial hypertension

Without intracranial hypertension

of the fungus, and lumbar puncture will reduce the fungus, though it may quickly re-form.

An alternative hypothesis (O'Connell, 1943 a and b) attributes this form of cerebral fungation to the giving way of the injured, softened wall of the lateral ventricle before the rhythmic pressure fluctuations which occur within the ventricle. Those pressure fluctuations have been shown to be of considerable magnitude and it is believed that they are an important factor in the production of the localized hydrocephalus which follows damage to an area of cerebrum from differing causes. When the cerebral injury is associated with a wide breach in the coverings of the brain the thinned and softened wall of the lateral ventricle continues to stretch before the thrusts of intraventricular pressure, and the cerebrum is thus carried through the dural defect with the formation of a progressively enlarging fungus (Fig. 181).

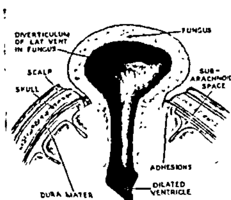


FIG. 181.—Drawing indicating the hypothesis that progressive ventricular dilatation is the cause of certain cases of progressive cerebral fungation.

4. MORBID ANATOMY

When a missile penetrates the brain the subarachnoid space around the margins of the track is usually rapidly obliterated by adhesions. Cerebral tissue protrudes through the dural opening into the superficial wound. The appearance of the lesion varies. In the early period after wounding the fungus consists of a mixture of haemorrhagic brain tissue and blood clot. It is soft and may adhere to, and be removed with, the dressings. With the advent of infection a change occurs. If the infection be of an early virulent kind it gives rise to a rapidly enlarging soft haemorrhagic fungus which is malodorous, and bubbles of gas may escape from its surface. In other cases in which the infection is localized to the track of the missile, the protrusion will at first have the appearance of cerebral tissue, and will later gradually be converted into granulation tissue. In some cases, on its surface there will be found the orifice of a track from which a discharge of pus occurs, but in other cases no such track can be found. With the conversion of the exposed cerebrum into healthy granulation tissue epithelialization from the margins of the scalp wound occurs.

Important factors in production

Thus it will be seen that two important factors in the production of a brain fungus are (1) the presence of a wound and (2) some factor which leads to the protrusion of cerebral tissue through this to the exterior. A third factor is the nature of cerebral tissue. It is relatively soft and unresisting and its content of fibrous tissue is low. It is therefore readily displaced out of the cranium and, since its replacement by granulation tissue is slow, it remains in the wound as obvious brain tissue when the surrounding scalp and pericranium are granulating well. When the fungus itself granulates it becomes more rigid and the tendency for progressive protrusion to occur diminishes.

5. CLINICAL PICTURE

In the case of a penetrating cerebral wound, seen early, the fungus is of significance only as an indication that the cerebrum has been penetrated. After débridement and suture of the wound it ceases to exist. In the rapidly growing malodorous fungus associated with a virulent infection the appearance is characteristic. The patient is usually acutely ill, confused and restless and, unless the infection can be combated, likely to die in coma within a short period.

Localized infection

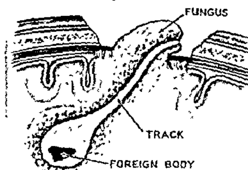


FIG. 182.—Drawing of an infected penetrating brain wound showing cerebral fungus.

In the group of cases in which infection of a localized type is present in the wound, either because of inadequate débridement or because early surgery has not been available, the patient will frequently show evidence of intracranial infection. This may take the form of pyrexia, meningeal irritation or a cerebrospinal fluid pleocytosis. Frequently, as has been seen, the orifice of a track will be found on the surface of such a fungus (Fig. 182).

No evidence of intracranial infection

Finally, there is the group of cases in which no evidence of an intracranial infection may be present and in which intracranial pressure is normal, and yet a progressively enlarging fungus is present. In such cases the wound of the cerebral coverings is frequently extensive and the surface of the fungus is smooth—no track being found leading into it. Patients with these extensive wounds will often show a gross functional neurological deficit and, in addition, are prone to attacks of meningeal irritation, in which the cell content and protein content of the cerebrospinal fluid are increased although no organisms are present in it.

6. TREATMENT

This will vary with the type of fungus. That seen in the early post-traumatic period will be treated by wound excision and closure as soon as possible. In the second group of cases in which fungation is due to infection, such a radical attack would be unwise. Here if an actual brain abscess exists it must be localized and treated by one of the recognized methods. Drainage will frequently be the most suitable technique, and repeated post-operative lumbar puncture will frequently be found helpful in maintaining drainage. In infected cases in which a track is present, repeated lumbar puncture will often dilate the track and thus permit of efficient drainage, and even the removal of contained bodies (Fig. 183). It has already been indicated that prognosis is bad in the case of early virulent infection with fungus formation. Radical removal of infected tissue together with local, intrathecal and systemic penicillin would perhaps enable some patients in this group to survive.

Drainage

Finally, there are the cases of progressive cerebral fungation in which no underlying infective cause can be found. Here the process must be controlled

by cerebrospinal fluid drainage—usually by lumbar puncture. It is essential that the drainage be thorough, the cerebrospinal fluid pressure being reduced to zero. If this drainage is allowed to take place slowly, resultant headache is diminished. It must be repeated at least once a day and perhaps over a period of many weeks. The effect of lumbar cerebrospinal fluid drainage on fungi of this type is indicated in Fig. 184. With the collapse of the lateral ventricle and its diverticulum a large fungus may be converted into a deep concavity. Fig. 184 also indicates another point which may be helpful in treatment. The granulating fungus tends to adhere to the granulating edges of the scalp and skull defect; such adhesions may prevent the accomplishment of full reduction of the fungus by lumbar puncture. If the adhesions are separated by gentle stroking with cotton pledgets the benefits of lumbar puncture may be increased.

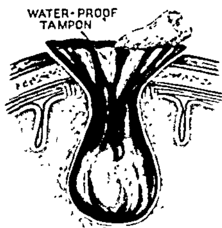


FIG. 183.—Drawing indicating the effect of repeated lumbar puncture in opening the missile track in wounds such as that illustrated in Fig. 182, and also treatment by tamponade.

Local treatment of the wound will be directed to minimizing injury to the nervous tissue and infection in the wound. To this end penicillin or sulphanilamide powder is applied locally, followed by a non-adherent dressing. *Penicillin application* Systemic chemotherapy will also be wise in the early stages and when symptoms arise which indicate it.

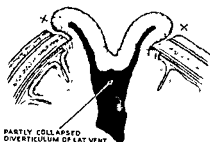


FIG. 184.—Drawing indicating the effect of lumbar puncture in progressive cerebral fungation. Adhesions may form (at X) between fungus and scalp and should be gently separated.

In the later stages other forms of treatment may be required. If the fungus forms a wide granulating area, a Thiersch graft may speed healing (Dickson Wright, 1940). *Thiersch graft* The scar which lies beneath the epithelium covering a healed fungus is rigid, and cranioplasty may therefore be unnecessary. If the latter is indicated it will necessitate the excision of the thin epithelial covering of the brain and its replacement by a scalp flap. The bare area of pericranium so produced is covered with a Thiersch graft, and at a second operation cranioplasty is performed. In view of the dense cerebral scar which replaces a cerebral fungus it is not surprising that in many patients with this lesion epilepsy subsequently develops. In some of these, scar excision may be indicated to control or reduce the frequency of the attacks.

7. RESULTS OF TREATMENT

Treatment designed to control the spread of infection, remove the cause of the fungation and minimize brain injury should bring about healing of the wound in most cases. It is likely that at least some of the fungi due to early virulent infection form an exception to this statement.

Although the lesion itself is thus frequently curable it must be borne in mind that many of these patients have had severe brain wounds. It is to be expected, therefore, that residual functional defect will be frequent, and so too will be epilepsy due to cerebral scarring.

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[References to other titles are given under Brain—Fungus in the Index Volume.]

BRAIN—INJURIES AND COMPLICATIONS

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1. INTRODUCTION

74.] The era of motor transport has brought with it ever-increasing numbers of cranio-cerebral injuries. By virtue of modern highway systems cases may be widely dispersed, and surgeons everywhere must be familiar with the problems of diagnosis in acute brain injury, management of the uncomplicated case of cerebral concussion and contusion, and the recognition of complications requiring surgical intervention. A very small group of cases requiring operation to save life must be dealt with at once. This very small group must be differentiated from those patients who should not be operated upon unless all the resources and facilities of a modern neurosurgical unit are available. By modern resources are meant efficient lighting, efficient suction, electro-coagulation and a full range of neurosurgical instruments, on the one hand, and the requisite knowledge on the other. Sound neurosurgical nursing care following any operation is indispensable.

2. TRANSPORTATION OF COMATOSE AND SEMI-COMATOSE PATIENTS

Patients with cranio-cerebral injury stand transportation well. Indeed, patients lying semi-prone on a stretcher in a modern ambulance are in no way worse off than a patient lying in bed. There are but two main requirements for the successful transportation of semi-comatose or comatose patients. The first is that the patient shall not be rapidly sinking into deeper coma. The second is that the patient shall be nursed on a stretcher as he would be in bed, in a semi-prone position, with the chin directed towards the stretcher, the head supported on a pillow or a folded blanket, and a folded blanket or pillow placed between the stretcher and the chest. This allows the tongue to fall forward, preventing laryngeal obstruction; the inhalation of blood and mucus is avoided should there be bleeding into the pharynx from a fracture of the base of the skull. The preceding views as to the feasibility of transportation of patients, unconscious following brain injury, are supported by

Position for nursing the patient

experience with air-raid casualties during the Battle of Britain, and with wounds of the head in the British and Canadian Armies.

In every head injury the disturbance of cerebral function, with resulting loss of consciousness occurring at the moment of impact of force to the head, must be assessed when the patient is first seen. Understanding of the pathological processes responsible for post-traumatic coma or semi-coma following head injury is necessary for rational management of patients and the prompt recognition of complications requiring surgical treatment.

3. PART PLAYED BY CONCUSSION AND BY INTRACRANIAL SPACE-OCCUPYING LESIONS IN THE PRODUCTION OF COMA

(1) Immediate disturbance of consciousness caused by concussion

A state of unconsciousness or impaired consciousness, however fleeting, produced by the sudden application of mechanical force to the skull, is due to concussion. Knowledge has not been fully clarified regarding the transmission of force from skull to brain. The following mechanisms may be involved: linear acceleration or deceleration of the head (Denny-Brown and Russell, 1941); rotational acceleration of the head producing shearing-strain forces in the brain (Holbourn, 1943); the sudden production of waves of increased pressure spreading throughout the intracranial cavity asynchronously (Walker, Kollross and Case, 1944). Combinations of these mechanisms of transmission of force may occur, and indeed, additional and unknown mechanisms not mentioned above may later be proved important.

Cerebral concussion

Regardless of how force is transmitted from skull to brain, it must be appreciated that cerebral concussion is a patho-physiological cellular disturbance of the brain related to shaking up or vibration consequent on trauma to the head, without macroscopical or microscopical evidence of primary damage to brain cells. The depth and duration of coma, semi-coma or confusion in an uncomplicated head injury is dependent upon the severity of the concussion.

Walker and his co-workers, by studies of the electrical activity of the brain in animals, have shown intense excitation of the central nervous system at the moment of a blow to the head. This is followed by "extinction" of normal activity of the central nervous system. Patients and animals may die immediately following head injury because concussion has paralysed the function of the vital centres (respiratory, cardiac, vasomotor). Death may occur without evidence of contusion or laceration of the brain and without intracerebral haemorrhage. Recovery from concussion, that is from the effects of mass excitation of the brain followed by extinction and then disorganization of normal cerebral activity, should gradually occur if the vital centres were not overwhelmed at the moment of injury. The time necessary for recovery from uncomplicated concussion depends upon the severity of force transmitted to the brain, that is, upon the severity of concussion.

(2) Delayed deterioration of consciousness caused by intracranial space-occupying lesions

Deterioration of consciousness, hours, days or weeks, following head injury is almost regularly due to the development of an intracranial space-occupying

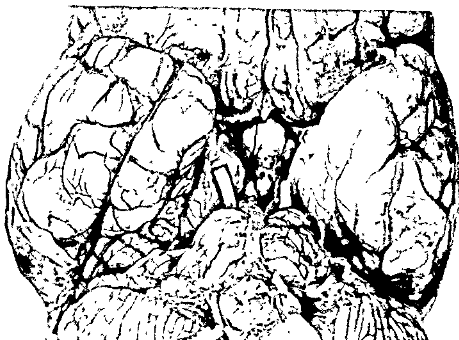


FIG. 185.—Note effects of tentorial herniation of right hippocampal gyrus and uncus. Oculomotor (third) nerve on right (outlined in ink) is compressed with resulting paralysis and a fixed dilated pupil. (*By courtesy of Professor E. A. Linell, Department of Neuropathology, University of Toronto.*)



FIG. 186.—Third nerve is pinned back on right; note crowding of hippocampal gyrus and uncus against midbrain. (*By courtesy of Professor E. A. Linell, Department of Neuropathology, University of Toronto.*)

lesion or to post-traumatic meningitis. Extradural, subdural or intracerebral clot, massive cerebral softening, or widespread cerebral oedema are the common causes of delayed deterioration of consciousness. An expanding supratentorial lesion leads to herniation of the temporal lobe (hippocampal gyrus), through the incisura of the tentorium (Jefferson, 1938). Hypothalamic and brain-stem function are disturbed both by direct pressure of herniated temporal lobe and by circulatory changes, chiefly venous. Consciousness deteriorates, leading to semi-coma and coma. Tentorial herniation of the hippocampal gyrus of the temporal lobe stretches the oculomotor (third) nerve (Figs. 185 and 186), leading to paralysis of the third nerve function with the development of a fixed and dilated pupil. Tentorial herniation, and later cerebellar herniation, acting on midbrain and brain stem, disturb, and finally paralyse, the function of the vital centres. The episode precipitating death in patients comatose because of tentorial herniation is commonly haemorrhage, of venous origin, in midbrain or pons (Scheinker, 1946). *Tentorial herniation*

With clear understanding that immediate disturbance of consciousness is dependent upon concussion, and that delayed onset of coma implies a space-occupying lesion of significant size, consideration can be given to some other immediate effects of head injury.

4. OTHER EFFECTS OF HEAD INJURY

(1) Contusion and laceration of the brain in the absence of a penetrating wound

The frequent occurrence of cerebral contusion immediately beneath the site of a blow to the skull combined with extensive contusion directly opposite the site of injury has long been recognized. The term *contre coup* will be used only to denote cerebral injury situated directly opposite the blow to the head. Bilateral contusion and superficial laceration of frontal poles, orbital surfaces of frontal lobes and temporal poles is a very common finding in patients with more than momentary loss of consciousness. Contusion and laceration may be more marked on one side than on the other, depending upon the situation of the blow to the head and the direction of force applied to the skull. Pudenz and Shelden (1943) by means of ultra-rapid moving pictures of a monkey with a lucite skull cap showed beautifully the movement of the brain during and following a blow to the head. The writer saw this film projected at normal speed and in slow motion, and was impressed with the rotational component of movement of the brain. Additionally, there was a ripple of movement through the brain as if a mould of jelly was tapped smartly. The rotational component, in support of Holbourn's (1943) hypothesis, would seem to play a substantial part in producing contusion of the temporal poles and the orbital surfaces and poles of frontal lobes. The frequency of injury in these regions is in itself strong evidence against any simple *contre coup* mechanism, for such injury occurs bilaterally when force is applied to the side as well as to the back of the head. *Movement of brain*

Cerebral contusion, either direct or *contre coup* in these situations, and with laceration and tearing of the pia, almost certainly plays no part in producing initial coma or semi-coma. Subarachnoid bleeding regularly results, the blood becoming mixed with the cerebrospinal fluid. Close relation between the

amount of bleeding and the degree of contusion and laceration is difficult to establish, for a small laceration may rupture a large vessel and produce substantial bleeding into the subarachnoid space. Generally, the more severe the head injury and cerebral contusion the more blood is found in the cerebrospinal fluid. Massive contusion and laceration of frontal or temporal poles may result in the formation of clinically significant space-occupying lesions. These are as follows: (1) Large intracerebral and peripolar subdural clots. (2) A large amount of softened, pulped, haemorrhagic brain. (3) Cerebral oedema spreading through the hemisphere, secondary to the presence of intracerebral clot and necrotic softened brain.

Space-occupying lesions

(2) Fracture of the skull

Fractures of the skull are of importance only inasmuch as the brain or cranial nerves may be directly or indirectly injured by the fracture or the fracture provides a source of potential brain injury.

Depressed fractures directly injure brain with and without penetration of the dura. Fractures traversing the paranasal sinuses, middle ear and mastoid air cells provide a potent source of meningitis should an accompanying tear of dura mater be present. Fractures crossing the groove or tunnel for the middle meningeal artery may tear the middle meningeal vessels, resulting in haemorrhage and the formation of an extradural haematoma. Similarly haemorrhage may result from a fracture tearing the sagittal sinus or lateral sinus.

In a general way it is reasonable to state that the presence of a long or wide linear fracture indicates substantial force applied to the skull. Every neurosurgeon of experience can recall vivid exceptions to this generalization for, on occasion, apparently minor force produces extensive linear fracture of the skull.

5. DIAGNOSIS AND INITIAL MANAGEMENT OF ACUTE BRAIN INJURY WITH COMA, SEMI-COMA OR MENTAL CONFUSION

A clear airway and unobstructed breathing

The first manoeuvre in dealing with any comatose or semi-comatose patient is the establishment and maintenance of clear, unobstructed respiration. Laboured breathing most commonly results from the tongue falling backwards and obstructing the larynx, because the patient is lying flat on the back. Laboured breathing produces cerebral congestion, predisposing to bleeding from contused, lacerated portions of the brain, and to cerebral oedema. Cerebral and general anoxia and cyanosis result. Easy, unobstructed breathing is produced by placing the patient semi-prone with the head supported by a pillow and the chin directed towards the mattress. The chest should also be supported by a pillow to allow easy excursion of the diaphragm. A rubber airway may be used for short periods, to prevent laryngeal obstruction. Blood coming from the nose, nasopharynx or mouth is often inhaled by the comatose or semi-comatose patient lying flat on the back. This is largely prevented by using the semi-prone position in hospital and during transportation. It may be necessary to suck out the trachea under direct vision, and even to aspirate the bronchi to relieve respiratory distress due to pulmonary atelectasis. The author has observed dramatic improvement following these procedures. In critically injured patients, disturbed function of vocal cords may

be the cause of laboured stertorous respirations. Consideration must be given to a tracheotomy in certain of these patients.

After establishment of unobstructed respirations the patient is examined to establish a base-line from which the future clinical course may be followed. Of primary importance is the level of consciousness. This must be described and recorded so that successive observers can decide whether the patient is recovering and the level of consciousness improving, or the patient is getting worse with deterioration of the level of consciousness. It is recommended that the definitions of coma, semi-coma and confusion put forward in "A Glossary of Psychological Terms Commonly Used in Cases of Head Injury" by the Medical Research Council, Brain Injuries Committee, should be utilized to facilitate accurate description of disturbed consciousness following head injury. *"Base-line" in terms of level of consciousness*

Coma.—"A state of absolute unconsciousness as judged by the absence of any psychologically understandable response (including, for example, change of expression) to external stimuli or inner need. Note: If a patient is comatose, it is important to record the state of activity and levels of nervous integration lower than that which is the substratum of consciousness. Such activities are reflex, such as swallowing, pupillary and corneal reflexes, tendon jerks, plantar responses." *Coma*

"It is not uncommon to hear it said of a patient who is comatose and cannot swallow that he is 'deeply unconscious'. This statement has no real value. He should be said to be comatose with loss of swallowing reflex."

Semi-coma—"A state in which psychologically understandable responses are elicited only by painful or other disagreeable stimuli, such as pinching the skin, shaking the patient vigorously." *Semi-coma*

Confusion (clouding of consciousness).—"Disturbance of consciousness, characterized by impaired capacity to think clearly and with customary rapidity, and to perceive, respond to and remember current stimuli; there is also disorientation. Note: When a patient is said to be suffering from confusion the degree should always be specified." *Mental confusion*

Record is made of temperature, pulse, blood-pressure and respirations as a measure of the function of the vital centres in brain stem and hypothalamus. These observations are charted at frequent intervals and a written record made of the rhythm and regularity of breathing. *Temperature, pulse, blood-pressure and respirations*

The head is examined for evidence of injury—(1) the presence of a contusion or contused laceration of the scalp, and (2) tenderness to localized deep pressure and swelling deep in the temporal region. These findings suggest an underlying linear fracture or the possibility of a depressed fracture. The site of a contusion or contused laceration of the scalp may be of considerable importance in the later diagnosis of massive cerebral softening or haemorrhage, *contre coup* in situation. The technique of dealing with scalp wounds has been put forward elsewhere, but it must be repeated that the presence of cerebrospinal fluid or pulped brain in a scalp wound is pathognomonic of a penetrating brain wound. The skull should be palpated carefully with a gloved finger through a scalp wound in search of depressed fracture. Scalp wounds should not be probed. Passage of a probe through a contaminated scalp wound into the brain provides an additional chance of introducing infection into the brain. *Examination of head*

Bleeding from nose or ears, rhinorrhoea and otorrhoea

Cerebrospinal fluid leak from the nose and cerebrospinal fluid leak or bleeding from the ears must be sought for and recorded as present or absent. In the absence of otorrhoea or bleeding from the ear, auroscopic examination is a routine measure, for bleeding into the middle ear may be present and will produce discoloration of the tympanic membrane. Any of these findings are strong clinical evidence of a fracture involving paranasal sinuses, mastoid air cells or middle ear. Indeed, bleeding from the nose or nasopharynx, in the absence of significant injury to face or nose, is strongly suggestive of a fracture involving the floor of the anterior fossa or sphenoid sinus. Clinical or radiological evidence of a fracture, compound into the mastoid, middle ear or paranasal sinuses, indicates a potential source of infection of the meninges and post-traumatic meningitis; in every such instance penicillin should be administered parenterally, 200,000 units in each 24 hours, and sulphadiazine given by mouth or stomach tube. The effective blood and cerebrospinal fluid levels should be obtained as rapidly as possible by giving an initial dose of 3 to 5 grammes of sulphadiazine and carrying on with 1 gramme every 3 to 4 hours, depending upon the level of drug in the blood. The use of sulphonamides should not be omitted, for post-traumatic meningitis has been observed to develop while two patients were receiving 160,000 units of penicillin daily by the intramuscular route. This routine should be carried out for 5 to 7 days following injury or for 3 to 5 days after the spinal fluid leak has stopped.

Prevention of post-traumatic meningitis

Local disturbance of brain function

Neurological examination, though limited by the comatose or semi-comatose patient's inability to co-operate, must be as complete as possible. A general survey of the restless patient may quickly indicate weakness or loss of usefulness of the extremities on one or other side; unilateral grimacing suggests contralateral facial weakness, and so on.

Papilloedema

Ophthalmoscopic examination of the fundi is important, for the presence of papilloedema is clear evidence of a pathological increase in intracranial pressure requiring special watch for deterioration of consciousness, due to an intracranial clot or massive cerebral softening. On several occasions the observation of papilloedema has been most helpful to the writer. It must also be appreciated that papilloedema is uncommon within 24 to 48 hours of a head injury, even in the presence of a fatal increase in intracranial pressure.

Pupillary reactions

The size and shape of pupils are compared, together with their reaction to light. The development of inequality of the pupils with unilateral impairment of reaction to light of the larger pupil and finally a fixed and dilated pupil, unreactive to light direct or consensual, indicates progressive damage of the third nerve culminating in paralysis. This sequence of events is strong evidence of tentorial herniation of the temporal lobe with stretching of the third nerve. By contrast, third nerve paralysis may be produced at the moment of injury by a shift of the brain stem pulling the third nerve out by its roots or by stretching it across the posterior cerebral artery. Injury and paralysis of the third nerve may also result from fracturing in the region of the basisphenoid or orbit. Finally, third nerve paralysis must be differentiated from a traumatic mydriasis associated with injury to the face and orbital region and involving the eye bulb. A traumatic mydriasis is unaccompanied by loss of external ocular movement or ptosis.

Mechanism of oculomotor paralysis

In brief, third nerve paralysis may be produced at the moment of injury or as a later development evidencing the presence of a supratentorial

space-occupying lesion producing tentorial herniation; differentiation depends upon careful examination by the first observers who see the patient soon after injury.

Unilateral blindness Absence of pupillary constriction to direct stimulation of the retina by light, with preservation of the consensual reaction to stimulation of the other eye, is indicative of blindness. This usually results from damage to the optic nerve and is accompanied by fracturing in the region of the optic canal.

Corneal reflex *Trigeminal nerves—fifth.*—The presence or absence of a corneal reflex is recorded; an absent reflex is commonly associated with serious disturbance of brain-stem function. Occasionally the fifth nerve and seventh nerve may be damaged at the moment of injury by fracturing of the petrous temporal bone.

Immediate facial paralysis *Facial nerves—seventh.*—The function of the facial nerve is recorded in terms of general emotional facial movements. It is tested in uncooperative patients by painful pressure on each supra-orbital nerve. Pressure on the supra-orbital nerve regularly results in that side of the face being screwed up. Facial paralysis may occur at the moment of injury due to involvement of the nerve by fracture in the petrous temporal bone. This is a rare occurrence and carries with it but slight chance of recovery of function of the facial nerve. The commoner form of post-traumatic facial paralysis is delayed in onset, and recovery is almost invariable.

Immediate facial paralysis of upper motor neurone type may arise from contusion of motor cortex.

Delayed facial paralysis Delayed facial paralysis is regularly associated with haemorrhage from the external ear or into the middle ear, and careful radiological studies of the mastoid region usually show a linear fracture entering the region of the petro-mastoid. Haemorrhage into the facial canal with compression of the facial nerve is probably the mechanism of production of delayed facial paralysis. Commonly, the onset is delayed for 1 to 4 days following injury. In a general way, the longer the delay in developing facial paralysis, the quicker is the recovery, the average time required being 1 to 3 weeks. Rarely, the nerve degenerates, when regeneration requires 3 to 4 months.

Power in arms and legs The function of the extremities with relation to power is gauged by the degree of general activity of the patient, by comparing the falling away of the outstretched arms and the response of arms and legs to a painful pinch on the inner side of arm and thigh. Tone is tested by manipulation of arms and legs.

Reflexes Comparison of the activity of biceps, triceps and supinator jerks in the arms, and of knee and ankle jerks in the legs is carried out. Superficial reflexes, the abdominal reflexes and plantar responses are compared. It is noteworthy that unilateral or bilateral extensor responses are commonly present shortly after brain injury producing semi-coma or coma, and become flexor in character as general improvement in cerebral function takes place. The importance is again stressed of accurate assessment of cerebral function observed on initial examination, so that "at once paralysis" due to local cerebral contusion and laceration will not be confused later with paralysis secondary to the formation of an intracranial space-occupying lesion.

Sensation Sensory function can be gauged only by the comparison of the responses to painful stimuli over corresponding areas, and assessment may be made difficult by the presence of weakness or paralysis of the extremities.

Radiological examination of the skull is performed immediately following

X-ray examination of the skull

clinical examination in all patients, save in those obviously fatally injured or excessively uncooperative or suffering shock from blood loss or other injury. A high percentage of satisfactory films is obtained by experienced radiographers even when the patient is restless and uncooperative. When adequate x-rays are considered essential, it may be necessary to administer Sodium Pentothal. Stereoscopic lateral, postero-anterior and half-axial views are taken, and when fractures involving the frontal or ethmoid sinuses are suspected Waters's views are indicated. The term "Waters's position" is derived from a paper by Waters and Waldron (1915). In taking these views the patient lies prone with the chin on the x-ray table, and the nose 1·5 centimetres from the table. The rays are directed perpendicular to the film. Similarly, special films of the mastoid may be necessary to show a fracture in this region.

The importance of the early clinical or radiological recognition of a fracture involving paranasal sinuses or mastoid has previously been emphasized in relation to the prevention of post-traumatic meningitis. A calcified pineal gland may be shifted, indicating the presence of an intracranial clot or massive cerebral oedema, which is predominantly unilateral. Pneumo-cranium may have occurred. A fracture line may cross the groove of the middle meningeal artery, requiring special watch for the development of an extradural clot. Finally, penetration of the skull with a depressed fracture that is not suspected clinically may be demonstrated.

Lumbar puncture

Lumbar puncture should not be routinely performed. Information regarding intracranial pressure as gauged by manometric measurement, together with cytological and chemical studies of the cerebrospinal fluid rarely provide essential aid to diagnosis. If a patient is sufficiently restless to require forceful restraint while lumbar puncture is carried out, this procedure is contra-indicated. When an intracranial clot is suspected, lumbar puncture is contra-indicated, for tentorial herniation of the temporal lobes or cerebellar herniation through the foramen magnum may be precipitated, making a fatal outcome inevitable. The intracranial pressure as judged by lumbar puncture in cases of cranio-cerebral injury has been the subject of considerable debate. Various authors report studies of cerebrospinal fluid pressure in severe, closed head injuries. Disagreement exists regarding the frequency of pressures of over 200 millimetres. In many cases a high pressure is accounted for by restlessness and struggling on the part of these patients. In general it may be said that a high pressure reading—over 200 millimetres—in a restless patient is in itself of little significance and that the level of consciousness provides a more reliable index of the patient's welfare.

Lumbar puncture may be of value when a head injury occurs with a fit or in an intoxicated patient. Blood in the cerebrospinal fluid supports the presence of a cerebral contusion and laceration. Similarly, a record of blood in the cerebrospinal fluid may be useful for medico-legal purposes.

Blood in cerebrospinal fluid

Blood in the cerebrospinal fluid clears in from 5 to 7 days following cessation of subarachnoid bleeding, the cerebrospinal fluid becoming xanthochromic and then clear. Bloody cerebrospinal fluid results in meningeal irritation with stiffness of the neck, a positive Kernig's sign, and sometimes photophobia.

Associated injuries

Careful examination for injuries of a general nature must be routinely carried out. In particular, fracture dislocations of the cervical spine not infrequently accompany brain injury with coma or semi-coma.

6. CLASSIFICATION OF PATIENTS WITH ACUTE BRAIN INJURY

All patients with acute brain injury may conveniently be divided into three main groups, in relation to the level of consciousness existing from 10 to 20 minutes following injury. This interval, commonly, is the time elapsing before a patient is first seen by a doctor.

Group 1: Conscious when first seen.

Group 2: Comatose, semi-comatose or confused when seen.

Group 3: Critically ill with decerebrate rigidity.

Grouping patients in this fashion allows first the consideration of the management of cases with *uncomplicated cerebral concussion and contusion* of varying severity, and secondly, the recognition and management of complications requiring specific or surgical management may be considered. Appreciation of the usual course following brain injury due to concussion and cerebral contusion is necessary for the recognition of complications.

7. MANAGEMENT OF UNCOMPLICATED CASES OF CEREBRAL CONCUSSION AND CONTUSION

(1) Group 1. Conscious when first seen

This group constitutes the majority of all patients with brain injury. Such patients are but momentarily dazed or unconscious, due to concussion, and have momentary post-traumatic amnesia. It must be emphasized that this group *of patients requires just as careful initial assessment as does the confused or* semi-comatose individual, including x-ray examination of the skull. In every instance such cases should be under close observation for a period of 24 hours, so that careful watch may be kept for the delayed onset of deterioration of consciousness, indicating intracranial clot. Patients should be roused at hourly intervals throughout the night, and careful records of temperature, pulse, respiration and blood-pressure should be kept.

Management of mild concussion

With momentary post-traumatic amnesia a healthy adult patient should be *fit to return to work within a few days and rarely requires more than two* weeks off work. There is no need for these patients to be kept in bed and, in fact, activity should be encouraged after the first day.

Depressed fracture is more common in this group of patients with but momentary loss of consciousness than when coma and semi-coma are prolonged. Extradural haematoma, rare as it is, develops more commonly in this group *than in patients with* prolonged semi-coma. A second cause of delayed onset of mental confusion and semi-coma, accompanied by increase in temperature, stiff neck and Kernig's sign, is post-traumatic meningitis. Both extradural haematoma and post-traumatic meningitis occur after a lucid interval, typically hours in length, but sometimes days may elapse before the pathological process becomes manifest.

A late complication developing in this group of cases is chronic subdural haematoma. In a very small percentage of these cases chronic subdural haematoma becomes manifest 2 to 4 months following injury. Relatives of patients should be advised to bring the patient for a re-check examination

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should alarming symptoms, such as confusion, disorientation, severe headache or the like, develop in the months following injury.

(2) Group 2. Confused, semi-comatose or comatose when seen

(a) Management of patient during post-traumatic confusion

Management of patients from the stage of initial coma, during semi-coma and until the clearing of post-traumatic confusion requires (i) maintenance of as nearly normal a metabolic state as possible; (ii) prevention, or early recognition and treatment of intracranial complications.

Maintenance of normal metabolic state

The restless, semi-comatose patient, writhing about the bed and struggling against restraint, expends large quantities of energy. The patient frequently is unable to swallow as a result of disturbed function of the pons and medulla. Dehydration rapidly develops, followed by the effects of starvation, and both are aggravated by the endless activity. Within 12 to 24 hours of injury fluids must be provided and, if nutrition is to be maintained, an adequate caloric intake also. By means of a duodenal or gastric tube passed through the nose 2,000 to 2,500 cubic centimetres of fluid containing 2,000 to 2,500 calories is administered in each 24 hours after the first day. The requisite number of calories is supplied by 100 grammes of protein, 100 grammes of fat and 250 grammes of carbohydrate.

Nursing care

Excellent nursing care is of paramount importance. Fever caused by central disturbances of the heat-regulating centre requires that the patient be covered only by a sheet. It is a common experience to see a semi-comatose patient, bundled in blankets, with a fever of 103–105° F. per rectum, and to observe the temperature fall to 100–101° F. simply as a result of removing the blankets. The comatose patient is nursed in the semi-prone position and regularly turned to prevent the development of pressure sores.

The head of the bed is elevated 4 to 6 inches. The restless patient may require lubrication of the skin with oil, and bandaging of knees, elbows and ankles to prevent excoriation and brush burns. Sedatives, such as paraldehyde, 3 to 6 drachms, given per rectum or by duodenal tube, or Sodium Luminal, 3 grains intramuscularly or intravenously, may be used at intervals to control restlessness. Restraint is not used, for it aggravates the uncomprehending struggles of semi-comatose and delirious patients. The hands may be wrapped in generous amounts of cotton-wool, bandaged, and then covered with stockinet taped to the wrists. This prevents the patient from removing dressings, scratching the skin from chest or abdomen, pulling out a nasal tube or taking hold of nurse or attendant. A prolonged bath at body temperature does much to allay restlessness. Benefit often accrues from assisting a patient who is clambering about the bed, to walk up and down the ward or corridor till he is fatigued.

Restlessness and the distended bladder

A patient may be trying to get out of bed in order to urinate, and his restlessness will not abate until the bladder is emptied. Repeated examinations are made to ensure that distension of the bladder is not the cause of restlessness.

No concern is felt regarding the absence of a bowel movement for 3 to 4 days following injury. After this interval, or later, magnesium sulphate is given by mouth or tube, or an enema may be administered.

Rehabilitation of patients following brain injury presents problems common both to closed head injuries and to cases requiring operation. Convalescence

may be defined as starting when full consciousness has been regained and post-traumatic amnesia has ended.

(b) Treatment of patient following subsidence of post-traumatic delirium

From the earliest stage at which islands of memory may occur or fragments of conversation may be understood or remembered, every effort must be made by those in attendance upon the patient to carry out reassurance regarding ultimate recovery. The opposite is of equal importance, and unguarded remarks concerning a bad fracture of the skull or laceration of the brain must never be made in the hearing of a patient. For reassurance to be convincing to the patient, doctors, nurses and orderlies must appreciate what remarkable recovery commonly is made by a healthy young adult, even after days of delirium and incontinence.

All patients are encouraged to assume any position they desire in bed, and the head of the bed is regularly propped up. No attempt is made to induce the patient to lie flat in bed. Prolonged rest in the supine position predisposes to vasomotor instability with consequent dizziness and light-headedness on sitting up or standing up (McKenzie, 1943; Botterell and Wilson, 1944). When dizziness does result from sitting up, the head of the bed is elevated by degrees and kept elevated by day and by night.

As soon as there are no spontaneous complaints of symptoms such as headache and sufficient co-operation can be obtained, physical exercises are started while the patient is in bed. Tension exercises with deep breathing are carried out several times a day for short intervals under the supervision of a physiotherapist. Efficient performance of tension exercises without the development of symptoms should be achieved in most cases before the patient is allowed up. Finally, increasing activity about the ward is encouraged and reassurance continued regarding the lack of significance of fatigability, the association of headaches with fatigue, and lack of capacity to concentrate. Each case must be completely assessed and at an opportune time explanation is made to the patient that recovery is the rule, and that permanent disability, such as nerve deafness, must be accepted. The surgeon must be entirely convinced in his own mind concerning the patient's welfare, and continue close supervision and reassurance throughout the various phases of recovery. To encourage a patient to undertake more than he is capable of achieving without undue difficulty is as harmful as prolonged inactivity.

Exercises

Never is a patient asked directly if headaches are troublesome and, indeed, apart from the period immediately following post-traumatic amnesia, headache has not been a commonly troublesome symptom (Guttmann, 1943a).

Post-traumatic headache

Great benefit has resulted from the close collaboration of the neuropsychiatrists in the treatment of head injury. The early recognition of pre-existing or post-traumatic neurosis and other psychiatric states aggravated by or due to head injury has allowed prompt treatment of these patients. Mental retardation or permanent deterioration is assessed. The "post-traumatic syndrome" is so commonly a mixture of the organic effects of brain injury, with post-traumatic neurosis and aggravation of pre-existing personality defects, that assessment and treatment of this syndrome is primarily the responsibility of the neurologist. In all cases consideration must be given to the presence of a subdural haematoma or hygroma, and if necessary pneumo-encephalography,

Mental and emotional status following head injury

Post-traumatic syndrome

ventriculography or exploration through burr holes may be performed.

In the opinion of the writer, the most efficient diagnostic evaluation and treatment of the "post-traumatic syndrome" of headaches, dizziness, inability to concentrate, fatigability and mental retardation, is carried out by the neurologist; he requires the close collaboration of surgeon, electroencephalographer and radiologist, specially trained in the interpretation of pneumoencephalograms and ventriculograms if the patient is to receive maximal benefit.

(c) Duration of disability following brain injury

To generalize regarding the time required for recovery and return to work following brain injury is difficult and may be misleading. In a general way, the duration of post-traumatic amnesia as put forward by Symonds and Russell (1943) has proved to be the most satisfactory yardstick. However, a case of short post-traumatic amnesia with accompanying contusion of the motor region, with weakness of an arm or leg, may require prolonged time off work. With these qualifications the following figures are put forward only as a guide to time off work after a brain injury. This Table is based upon the work of Cairns (1942a), Guttmann (1943b) and Botterell and Wilson (1944).

Duration of post-traumatic amnesia	Estimate of shortest time before return to full work is possible
5 minutes to 1 hour	2 to 6 weeks
1 to 24 hours	6 to 8 weeks
1 to 7 days	2 to 4 months
over 7 days	2 to 8 months

It is noteworthy that the patient must be allowed to progress at his own rate in the days following a period of post-traumatic amnesia. Healthy adults recover more rapidly and completely than aged, somewhat arteriosclerotic individuals.

Prevention or early recognition and treatment of intracranial complications

Accurate initial assessment leads to the prompt recognition of depressed fracture and potential sources of meningitis, such as fractures involving paranasal sinuses or petro-mastoid. Initial assessment establishes the depth of coma due to concussion, and local disturbances of cerebral function due to concussion and local contusion or intracerebral haemorrhage. The course of an uncomplicated case of cerebral concussion and contusion consists of recovery of consciousness, the rate of progress depending upon the severity of concussion. Local disturbances of cerebral function due to concussion and local contusion, and manifest by hemiparesis or the like, also tend to improve steadily.

Clinical signs of complications

Repeated examination must be carried out, so that deterioration of consciousness, papilloedema, pupillary changes, increasing weakness and changes in reflexes may be recognized early. Such clinical changes may be the indication of an intracranial haematoma, subdural, intracerebral or extradural, of massive cerebral softening, and rarely, of widespread cerebral oedema. Cerebral oedema must never be accepted as the cause of secondary

deterioration of consciousness until intracranial clot and massive cerebral softening have been excluded positively by exploration through burr holes.

As pointed out with reference to Group 1, post-traumatic meningitis is also a cause of delayed or secondary coma.

(3) Group 3. Critically ill with decerebrate rigidity

The comatose patient, with rapid, irregular or periodic, stertorous breathing, with pulse so rapid as to be almost uncountable and low blood-pressure, with hyperthermia (103°–106° F.), and with decerebrate rigidity, presents an unmistakable picture of profound injury to brain stem and vital centres. Easy breathing often cannot be achieved even with a rubber



FIG. 187.—Multiple petechial and gross haemorrhages in midbrain of "critically ill" patient with decerebrate rigidity, hyperthermia, etc.; similar haemorrhages were present in the pons, and neighbourhood of the lateral and third ventricles.

airway in place, and tracheotomy must be considered in the light of the patient's general condition. Hyperthermia may be missed unless rectal temperatures are taken, for the extremities often are cold and cyanosed. It is combated by covering the patient with a wet sheet only, and turning on an electric fan. Aspirin 20 grains every 1–2 hours may be given by tube, as necessary, for 24 hours. Iced colonic irrigations are the final measure to reduce body temperature. Rectal temperature must be maintained below 103° F.

Duodenal feedings are instilled every hour, or by drip, in an attempt to prevent acute ulceration with secondary haemorrhage or perforation of the stomach or lower end of the oesophagus.

Survival requires intensive nursing care as outlined previously. Recovery is exceedingly slow and mental retardation, spasticity of the extremities and

disturbance of speech—dysarthria and the like—may persist for months. Children make more complete and rapid recovery than adults.

Mortality rate after severe injury

A minimal mortality rate of 50 per cent is encountered in this group of cases. Post-mortem studies show, in many instances, multiple petechial haemorrhages, sometimes more massive haemorrhage, in the pons, medulla, midbrain and the region of the third ventricle (Fig. 187). Whether these haemorrhages result directly from the primary injury or are secondary to cerebral vaso-paralysis and anoxia is as yet unsettled.

8. COMPLICATIONS OF BRAIN INJURY—EARLY

Complications of brain injury, other than cerebral concussion and contusion occurring in a closed head injury, may be regarded as pathological processes impeding recovery or endangering life. Experience with thousands of cranio-cerebral injuries in many centres has led to the recognition of signs and symptoms denoting complications which require specific or surgical treatment. The chronological sequence of events following brain injury, as shown by history and repeated physical and radiological examination, and lumbar puncture and cerebrospinal fluid examination when necessary, makes possible early and accurate diagnosis of intracranial lesions requiring operation. Surgery is carried out following brain injury only because some specific lesion is suspected. The era of indiscriminate subtemporal decompression has passed.

(1) Depressed fracture

A depressed fracture with an indriven punched-out area of comminuted bone results from the application of force to the skull by a fairly small mass of high velocity and small area of impact. Shell fragments, bits of brick, the head of a hammer, a knife blade, the point of a skate and the end of a steel fishing-rod are but a few examples of weapons capable of producing penetrating wounds. The force exerted by these small masses of high velocity is in large part used up in penetrating the skull. Local laceration of brain results, but force is not transmitted to the brain generally. It follows that concussion commonly is not a feature and consciousness is not lost or is, at most, momentarily impaired. However, violent force may produce a stellate depressed fracture and severe concussion with prolonged coma.

Local cerebral contusion and laceration

More often than not the fracture is compound with an overlying scalp wound. The inner table of the skull is usually more extensively fractured than the outer table. Whereas the dura and brain may or may not be directly lacerated by indriven bone fragments, cerebral contusion commonly occurs deep to an intact dura. Clinical evidence of local disturbance of brain function depends upon the area of cortex involved (motor, sensory, visual, and so on), and may be lacking in the case of the prefrontal regions, or right temporal lobe in right-handed individuals. Signs of increased intracranial pressure most often result from the combination of spreading cerebral oedema secondary to the presence of swollen pulped brain. Intracerebral, subdural and extradural clot do form but are relatively infrequent.

Diagnosis

Examination of all scalp wounds for the presence of pulped brain or cerebrospinal fluid, palpation of exposed skull with the sterile, gloved finger and

routine x-ray examination of the skull following initial examination lead to prompt diagnosis (Fig. 188).

(*a*) *Compound*

In all compound depressed fractures treatment consists of operation promptly carried out. Triradiate incisions must be avoided. All damaged and contaminated scalp, pericranium, skull and dura are excised. All pulped brain and indriven bone fragments are removed and absolute haemostasis must be achieved (Figs. 189 and 190). The dural defect is closed with split dura, pericranium, temporal fascia or fascia lata. In every case the scalp must be closed without tension. Single or double rotation scalp flaps may be necessary to close a defect (Gillies, 1944). Drainage should not be employed.

In selected cases with a minimum of brain injury and without clinical evidence of infection in the wound, tantalum cranioplasty may be performed at the primary operation.

Penicillin, 200,000 units daily, should be administered parenterally for 5 to 7 days following operation, together with sulphadiazine in full doses.

Efficient removal of pulped brain and complete haemostasis may prove an exceedingly difficult technical procedure in deeply-penetrating brain wounds. To avoid infection and formation of a cerebral abscess, to minimize scar formation and the likelihood of post-traumatic focal epilepsy, and to save life, these cases should be transferred, whenever possible, to the nearest centre equipped and staffed for neurosurgery. Preliminary treatment should consist only of the application of a sterile dressing to the scalp wound, the measures necessary to combat shock and haemorrhage and the institution of a regimen of penicillin and sulphadiazine. Delay of 1 to 3 days unless the patient is rapidly becoming comatose is less dangerous than a primary incomplete operation.



FIG. 188.—Compound depressed fracture in left frontal region; consciousness was momentarily lost; the dura was not torn; the left arm showed some weakness for a few days. (*By courtesy of the Department of Radiology, Toronto General Hospital.*)

(*b*) *Simple*

Simple depressed fractures, if seen early—up to 3 days—should be operated upon and the fragments elevated and replaced; if seen later, decision regarding operation rests chiefly on cosmetic and psychological grounds.

Depressed fractures involving frontal sinuses will be discussed under the

heading "Fractures involving paranasal sinuses" and "Post-traumatic meningitis".

(2) Extradural haematoma

Massive extradural haemorrhage *requiring surgical removal is* found most frequently in the "trivially injured" group of patients who are conscious when first seen. Emphasis must also be placed on the fact that extradural haematomas are found in patients who are semi-comatose when first seen. Massive extradural haemorrhage probably occurs in from 1 to 2 per cent of cases of acute brain injury. Accurate estimation of the incidence is difficult, for diagnosed cases are referred to neurosurgical centres, and not a few patients die of unrecognized extradural haemorrhage.

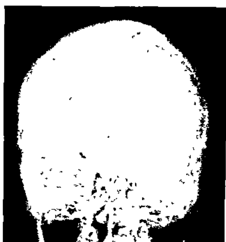




FIG. 189.—Parietal parasagittal penetrating wound, due to mortar-bomb fragment; paralysis of *both* legs, most marked below knees, with cortical sensory deficit—operation 3 days after injury; haemostasis required clipping two large parasagittal veins and a good-sized branch of the anterior cerebral artery; sagittal sinus was intact; 12 bone fragments were removed; healing was uneventful.

(*a*) *Source*

Tearing of the middle meningeal vessels—artery and venae comites—by *linear* fracture is the common source of extradural clot. The tear usually involves the anterior branch of the middle meningeal vessels, and the clot is situated over the temporal and lower Rolandic regions, though some tears are high, and clot may extend over the cerebellum also. Bleeding following laceration of the sagittal or lateral sinus may produce extradural clot of significant size. Particularly is this the case when obstructed respirations lead to venous congestion and a great increase in venous pressure.

Bleeding from diploic veins opened by fracture, and tearing of middle meningeal vessels in the absence of fracture are verified, though rare, causes of extradural haematoma.

(*b*) *Diagnosis*

Middle meningeal haemorrhage

Apparent complete recovery following momentary loss of consciousness, succeeded in a few hours—the lucid interval—by headache, confusion, semi-coma, coma and death, is the typical history of a case of middle meningeal haemorrhage. As coma deepens, respirations and pulse rate slow down, finally rising with accompanying hyperthermia. Operation should be performed before the development of rising pulse rate, respiratory rate and temperature, which are serious signs.

Examination during the development of stupor may disclose three lateralizing signs: *Lateralizing signs*

(i) Oedema of the scalp or swelling deep in the temporal fossa, suggesting a linear fracture.

(ii) A dilating, or dilated, fixed pupil on the side of the lesion, secondary to tentorial herniation of the temporal lobe (hippocampal gyrus) and stretching of the third nerve against the sharp edge of the tentorium.

(iii) Disturbance of reflexes and diminution of movement of arm and leg due to pressure by clot on the underlying brain. Convulsions may result from pressure on underlying brain involving arm and leg on the opposite side. Because of semi-coma or stupor, weakness has to be demonstrated often by the response to painful stimuli.

Neither oedema of the scalp nor disturbance of reflexes and movement of the arm and leg are regularly present. Even dilatation of the pupil may be a false localizing sign in terms of its lateralizing value.

Whereas most frequently the initial injury is a slight one, and the lucid interval a matter of hours, there may be no lucid interval when extradural bleeding is rapid and complicates a severe brain injury; the comatose patient may recover to a restless stage of semi-coma, later relapsing to coma and dying; rarely, the lucid interval may be of many days' duration before headache, mental confusion and papilloedema lead to exploration and treatment (McKenzie, 1938).

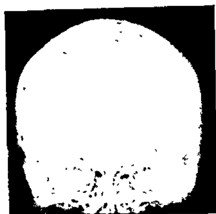




Fig. 190.—Post-operative film: note removal of in-driven fragments. Compare with Fig. 189.

Recognition of a pineal shift by x-ray examination in a patient with a long lucid interval provides positive aid in making the diagnosis. *Pineal shift*

(c) *Surgical treatment*

Treatment consists in exploration by burr holes at the moment an extradural clot is first suspected. Burr holes are regarded as a diagnostic measure and the only means of positively excluding intracranial haematoma as the cause of secondary deterioration of consciousness. The mortality from extradural haematoma increases markedly if operation is delayed till the diagnosis is beyond doubt.

Extradural haemorrhage constitutes a true emergency which any surgeon may be obligated to treat. The clot is evacuated by enlarging the exploratory burr hole deep to the upper mid-portion of temporal muscle rather than by turning a bone flap. The bleeding meningeal vessel may be controlled *Technique*

by *electro-coagulation*, by the application of a silver clip or by suture-ligation. In some cases it may be necessary to occlude the foramen spinosum with cotton-wool, or a bit of a wooden match or spatula. Lack of efficient suction or lighting, or generalized weeping of blood from a very vascular dura may make it impossible to obtain satisfactory haemostasis. Under such circumstances the extradural space should be packed with gauze and the wound sutured open by stitches from galea to scalp half an inch from the scalp edge. Lives have been saved by this manoeuvre.

Mortality rate

The mortality rate in extradural haematoma varies directly with the promptness of diagnosis and the degree of accompanying brain injury. Rarely do patients recover when tentorial herniation of temporal lobes has become sufficiently marked to produce bilaterally fixed and dilated pupils, with accompanying signs of failure of vital centres, rising pulse and respiratory rate and hyperthermia. There is a death rate of from one-third to one-half the number of patients with extradural haematoma admitted to hospital.

(3) Acute subdural and intracerebral haematoma

(*a*) *Source*

Severe cerebral concussion and contusion may be complicated in the days following injury by the effects of unilateral or bilateral subdural haemorrhage of significant degree, that is, more than 3 millimetres in depth. This may originate from *contre coup* laceration of frontal or temporal regions of brain with rupture of cortical vessels and torn arachnoid (Botterell and Stewart, 1942), from tearing of veins crossing the subdural space to enter the venous sinuses, or from a torn sagittal or lateral venous sinus. Among 515 consecutive cases of accidental head injury admitted to a neurosurgical centre, there were 35 cases of subdural or subdural and intracerebral haematoma.

Incidence

Blood may spread over the whole lateral surface of the hemisphere in the unpartitioned subdural space, or may clot and collect chiefly round the temporal or frontal pole with, in addition, intracerebral haemorrhage and haemorrhagic cerebral softening (Figs. 191 and 192). Subdural clot develops in the absence of fracture of the skull. Indeed, in cases of suspected subdural clot, the presence of linear fracturing is useful chiefly in judging the site of injury to the head with reference to the possible site of *contre coup* contusion and laceration of brain and subdural intracerebral bleeding.

(*b*) *Diagnosis*

Diagnosis must be based on careful study of the march of events with reference to the *level of consciousness*, the *function of vital centres*, *evidence of* local disturbance of cerebral function and the detection of a dilating pupil.

Increased intracranial pressure

Increasing headache, papilloedema and increasing drowsiness, becoming manifest in the days following injury, are evidence of pathological increase in intracranial pressure. These signs may be accompanied by slowing of pulse and respiration. The development of secondary coma may take place over several days or may occur rapidly, requiring only a few hours.

Convulsions of focal origin, increasing dysphasia, unilateral weakness of arm and leg and disturbance of reflexes serve to lateralize and localize the situation of the clot. Visual field defects are rarely present. It must be stressed that clinical signs of localizing, or even lateralizing value may be absent or

very slight in the early stages. Unilateral dilatation of a pupil, or skiagrams of the skull showing lateral shift of a calcified pineal gland, may provide the only clue to the side of the lesion.

Cerebral fat embolism must be considered in the diagnosis. The presence of other injuries, particularly a fracture, petechial haemorrhages in skin or mucous membranes, blood-stained sputum, signs of moisture in the lungs, a dropping blood haemoglobin and fat in the urine, are salient clinical features. *Cerebral fat emboli*

(c) *Surgical treatment of subdural haematoma*

Chiefly of pathological interest is the discovery at necropsy of an unsus-

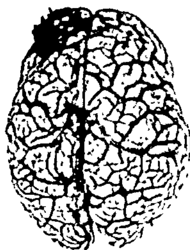


Fig. 191.—Intracerebral clot with rupture of cortical vessels and formation of diffuse subdural clot resulting from force applied to right occiput. Evacuation of subdural clot was ineffectual and patient died 10 days following injury. At necropsy no clot was present over hemisphere but a substantial amount had collected beneath orbital surface of frontal lobe. (*This illustration is from a paper in preparation for publication, in collaboration with Lt.-Col. O. W. Stewart.*)



Fig. 192.—Section through brain, same specimen as Fig 191, showing extent of intracerebral clot in the left frontal lobe, and swelling of the left cerebral hemisphere. (*This illustration is from a paper in preparation for publication, in collaboration with Lt.-Col. O. W. Stewart.*)

pected diffuse subdural haematoma in the patient deeply comatose from cerebral concussion and contusion on admission to hospital, and dying within 12 to 18 hours without sign of recovery. By contrast, surgical exploration is mandatory in cases admitted semi-comatose, responding to painful stimuli, who recover consciousness in some degree or maintain a steady level of consciousness for hours or days and then show deepening coma with or without evidence of local disturbance of brain function or pupillary changes. *Diffuse subdural haematoma*

The first step towards verification and evacuation of subdural clot is to rule out the presence of diffuse bleeding in the subdural space on the unlikely side,

for the lesion may be bilateral. This is done by means of a burr hole in the mid-temporal region immediately beneath the upper margin of the temporal muscle. If this is negative, the wound is closed in layers and a similar opening made on the other or suspect side. When clot is encountered, the burr hole is enlarged to the size of a silver dollar, the dural opening enlarged by cruciate incisions and the clot sucked out. Further burr holes are made in the frontal or parietal region, or both, depending upon the direction of extension of the clot, and the subdural space irrigated, by syringe and catheter, with saline. The incisions are closed in layers with soft rubber (Penrose) drains brought out from the subdural space, and hard rubber tubing brought out from the opening in the dura. Sutures are placed in the galea and skin, to be tied following removal of the hard rubber tube in 24 hours and the Penrose drain in 48 hours.

Mortality rate in acute diffuse subdural haematoma

The mortality rate is high with this type of lesion—associated as it commonly is with severe brain injury—approximating 50 per cent. In cases in which the brain injury is of minor degree and a cortical vessel has been torn with laceration of the arachnoid, operation is a life-saving measure.

(*d*) *Local temporal and frontal subdural and intracerebral clot*

The failure to find a diffuse subdural haemorrhage with bilateral burr holes in the upper temporal and parietal regions does not exclude a massive local subdural clot, with or without intracerebral clot and haemorrhagic softening of the temporal or frontal polar region. In fact, the major portion of clot, or haemorrhagic softening, may be within the anterior portion of the temporal or frontal lobe and the minor portion in the subdural space. These more localized haemorrhages are, as mentioned above, usually due to *contre coup* contusion and laceration of brain and cerebral vessels.

Exploration of temporal region

Exclusion of a diffuse subdural clot of significant depth must then be followed by exploration of the likely temporal lobe and adjoining region of the middle fossa in relation to the site of injury and clinical signs. This may be done by extending the incision for the temporal burr hole downwards to the level of the zygomatic arch, and cutting a channel in the skull approximately 2 centimetres in width down to the floor of the middle fossa. Additional bone is removed at the lower end of the incision and the dura incised over the temporal pole. Frequently, a collection of clot and pulped haemorrhagic brain extrudes under pressure and a "tight" brain slacks off; a peripolar or pancake clot may be encountered overlying the temporal lobe and arising from a superficial tear of brain and cortical vessels. Following evacuation of clot and damaged brain, a dry field is obtained and the wound closed save for a soft rubber (Penrose) drain in the subdural and intracerebral space together with a hard rubber drain extending down to the dural opening. The hard rubber drain is removed in 24 hours, the Penrose drain in 48 hours. The drainage tracks are closed by means of the tying of sutures which were inserted, but not tied, at the time of operation.

Exploration of frontal region

Exploration of the frontal region requires a burr hole immediately above the frontal sinus 3 centimetres from the midline, enlarged sufficiently so that the floor of the anterior fossa may be inspected.

There exists an alternative method of surgical treatment when the lesion can be lateralized with reasonable accuracy but not localized in temporal or

frontal region. A flap is turned down exposing the frontal lobe and anterior temporal region. The dura is opened only over the anterior-frontal and anterior-temporal regions. Clot and haemorrhagic pulped brain are evacuated as necessary.

Mortality rate

If operation is required within 24 hours, a high mortality rate, of the order of one-third to one-half, may be expected. Operation performed from 2 to 12 days following injury is accompanied by a greatly reduced mortality rate, and the survival of patients who previously deteriorated rapidly.

The exploration of temporal and frontal lobes for local subdural and intracerebral clot and pulped brain requires a complete neurosurgical establishment, for haemostasis may be difficult to achieve in the cerebral wound, and the post-operative course may be a complicated one.

(4) Acute subdural hygroma

Both in patients who are conscious when seen and those with more serious cerebral concussion, there is occasionally a valve-like tear in the arachnoid allowing one-way passage of cerebrospinal fluid into the subdural space. This results in the cystic collection of cerebrospinal fluid diffusely over the hemisphere. The fluid becomes syrupy and yellow and high in protein content —100 milligrams per cent or more. The intracranial pressure is raised and, depending upon the rate of accumulation of cerebrospinal fluid in the subdural space, coma and pupillary changes develop more or less rapidly. The pre-operative diagnosis is usually subdural haematoma. Treatment consists in exploratory burr holes and drainage for 24 hours. Recovery is the rule.

(5) Massive cerebral oedema

Diagnosis

Widespread cerebral oedema causing increased intracranial pressure and coma is rare in the absence of grossly damaged brain. A zone of swollen oedematous brain surrounds all areas of contusion and laceration containing softened necrotic brain. Experience with penetrating brain wounds and massive *contre coup* contusion of temporal or frontal lobes indicates that pulped necrotic brain swells and is capable of producing a fatal increase in intracranial pressure. The diagnosis of cerebral oedema causing secondary coma, following cranio-cerebral injury, cannot be accepted until extradural or subdural clot and hygroma, and massive contusion and haemorrhagic softening of temporal or frontal lobes have been excluded.

Positive exclusion of an intracranial space-occupying lesion can only be achieved by means of burr holes. Dehydration therapy should not be undertaken until this has been done.

The rare case of widespread cerebral oedema, unassociated with clot or cerebral softening and causing coma, occurs from time to time in every large series of head injuries. Twice—or three times—concentrated human plasma or serum administered intravenously in 500 cubic centimetre quantities at 3-hourly intervals, provides the best method of reducing cerebral oedema. Should serum or plasma be unavailable, 50 per cent glucose or 50 per cent sucrose may be used intravenously. The effect of glucose is not enduring and sucrose, though more enduring, may produce damaging effect on renal tubules.

Subtemporal decompression

The author believes that subtemporal decompression and the large bone

flap, with dura left open and bone flap unanchored, are so rarely of value in the treatment of brain injuries that they need not be considered here.

(6) Fractures involving paranasal sinuses

Fractures of the posterior wall of the frontal sinus, and the ethmoid sinus, establish communication between air sinuses and leptomeninges and brain when dura is torn. The threat of meningitis, subdural infection and brain abscess hangs over the patient, and intracranial sepsis may supervene hours, days or years following such an injury (Linell and Robinson, 1941).

(a) Occurrence

Fracturing of paranasal sinuses with torn dura and lacerated brain

Fracture of the frontal sinus or cribriform plate of the ethmoid may occur in patients with very minor concussion. Force applied to the zygoma, a relatively strong buttress, is transmitted diagonally across the thin roof of the orbit to the thinner cribriform plate, either of which may give way; the frontal sinus commonly extends into the roof of the orbit. Similarly, force applied to the nasal process of the frontal bone may produce fracturing of the frontal sinus or ethmoids.

Force applied to the vertex of skull, or the frontal bone remote from the frontal sinus or parietal region, may result in linear fracturing extending anteriorly to involve the posterior wall of the frontal sinus, or floor of the anterior fossa and ethmoids with comminution. Such cases generally have received a moderately severe brain injury and are semi-comatose or confused when seen. Linear fractures involving the posterior wall of the frontal sinus may pinch a tube of dura and arachnoid and, if accompanied by comminution, bone fragments may project from the posterior wall of the frontal sinus or ethmoid into the subarachnoid space or brain itself.

The most serious form of fracturing of the frontal sinus and ethmoid results from the application of severe force to the region of the frontal sinuses or supra-orbital ridges. This type of injury is commonly accompanied by severe fracturing of nose, malar bones and maxilla. Multiple fractures involve the frontal sinus and ethmoids, and comminution of ethmoids and roofs of orbits is always marked—more marked than is shown by x-ray examination. Fracturing may be compound from without, through both walls of the frontal sinus into the brain. The posterior wall of the frontal sinus and ethmoid may be comminuted, with tearing of the dura on the orbital surface of the frontal lobe and over the frontal pole; in fact there is compound fracturing from the frontal sinus and ethmoid into the brain. In extreme instances the supra-orbital ridge and ethmoid may be driven backward and crumpled, with accompanying fracture of nasal bones. The cribriform plate of the ethmoid may lie entirely free in the floor of the anterior fossa.

In such cases the anterior portion of the frontal lobe may be pulped and the dura extensively torn. The crumpled sinus may be filled with damaged brain tissue and, if compound to the exterior, brain may exude over the forehead. Pulped brain may escape through the nose.

Rhinorrhoea

Cerebrospinal fluid commonly escapes through the nose or into the nasopharynx when fracturing of paranasal sinuses is accompanied by a tear of the meninges. Escape of cerebrospinal fluid may be made difficult to recognize by accompanying bleeding or when the patient is lying in the supine position and cerebrospinal fluid is inhaled or swallowed.

(*b*) *Diagnosis*

Initial assessment, as outlined on page 356, requires a search for rhinorrhoea and bleeding from the nose. Rarely the escape of pulped brain from the nose may be observed. Observation of the patient, with the foot of the bed elevated 18 inches and the patient lying in the prone position may reveal a hitherto undisclosed rhinorrhoea.

Radiographic technique

Gross external frontal injury calls for x-ray films of the skull using stereoscopic postero-anterior views, and Waters's positions designed to show the frontal sinuses and ethmoid air cells, in addition to antero-posterior and lateral views. Accurate assessment of bony injury rests upon carefully taken and expertly studied x-ray films, and it must be emphasized that post-traumatic meningitis develops in the absence of recognizable rhinorrhoea.

(*c*) *Treatment*

The objective of surgical treatment is two-fold. (i) To prevent local infection at the site of injury and its spread intracranially in the acute phase following injury, and (ii) To deal with bony damage and torn dura so that the spread of infection from nose and paranasal sinuses to leptomeninges or brain will not occur in later months or years. To obtain this second objective it is generally agreed that a barrier must be created between air sinuses and brain in place of the damaged dura on the one hand, and that efficient drainage from frontal sinus and ethmoids must be established in spite of comminuted fracturing on the other hand. Some divergence of views (Cone, 1945; Cairns, 1942b; Schorstein, 1944) exists regarding the means of creating a barrier and establishing drainage, and it will be some years before sufficient time has elapsed to test long-term results.



FIG. 193.—Comminuted fracturing of right frontal sinus and right and left ethmoidal cells; brain escaping from right nostril; note facial fractures; Waters's position. (*By courtesy of the Department of Radiology, Toronto General Hospital.*)

It is generally agreed that adequate treatment for a linear fracture involving the posterior wall of the frontal sinus without evident comminution or rhinorrhoea consists of the parenteral administration of penicillin and sulphadiazine for 7 days following injury, and close observation with regard to the development of meningitis. The possibility is accepted that comminution may be present, though not shown by x-ray films, with the enhanced risk of meningitis in the acute phase and later.

Replacement of dura

For a comminuted fracture, in the absence of rhinorrhoea, many observers would be satisfied with a regimen of penicillin and a sulphonamide alone. In many such cases, Cairns, Calvert and their co-workers have, after a period of days, turned down unilateral or bilateral frontal flaps, replacing the dura by placing a graft of fascia lata extradurally, where necessary.

Many neurosurgical centres agree that this is the desirable course when

flap, with dura left open and bone flap unanchored, are so rarely of value in the treatment of brain injuries that they need not be considered here.

(6) Fractures involving paranasal sinuses

Fractures of the posterior wall of the frontal sinus, and the ethmoid sinus, establish communication between air sinuses and leptomeninges and brain when dura is torn. The threat of meningitis, subdural infection and brain abscess hangs over the patient, and intracranial sepsis may supervene hours, days or years following such an injury (Linell and Robinson, 1941).

(a) *Occurrence*

Fracturing of paranasal sinuses with torn dura and lacerated brain

Fracture of the frontal sinus or cribriform plate of the ethmoid may occur in patients with very minor concussion. Force applied to the zygoma, a relatively strong buttress, is transmitted diagonally across the thin roof of the orbit to the thinner cribriform plate, either of which may give way; the frontal sinus commonly extends into the roof of the orbit. Similarly, force applied to the nasal process of the frontal bone may produce fracturing of the frontal sinus or ethmoids.

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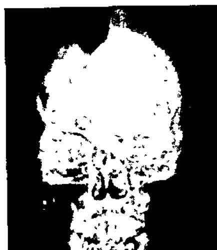
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(7) Post-traumatic meningitis

Septic meningitis following head injury is secondary to fractures involving paranasal sinuses and petro-mastoid, and to the development of sepsis in penetrating brain wounds; rarely is it the result of septic thrombophlebitis of emissary veins spreading deeply from an infected scalp wound. *Aetiology*

(*a*) *Pathology*



The organism most often invading the subarachnoid space from paranasal sinuses and mastoid is the pneumococcus. Pathways for the spread of infection are provided by a tube of dura and arachnoid pinched in a linear fracture of the frontal sinus, comminuted bone projecting into the subarachnoid space and brain, or fractured cribriform plate of the ethmoid.

Infection of a penetrating brain wound, with or without spread of infection and meningitis, reflects difficulty with primary surgical treatment. Removal of dead, pulped brain may have been inadequate because of a long narrow intracerebral wound track, possibly involving both hemispheres; in-driven bone fragments may be left in the brain wound, harbouring infection; inadequate débridement of scalp and temporal muscle may be responsible for superficial wound infection spreading deeply; failure to close the scalp wound without tension may result in necrosis of scalp, cerebrospinal fluid leak and meningitis.



Fig. 195.—Large collection of air in right frontal subdural space discovered 4 months following injury. (*By courtesy of the Department of Radiology, Toronto General Hospital.*)

Penicillin and the sulphonamides

The prophylactic use of parenteral penicillin and sulphonamides has reduced remarkably the incidence of meningitis due to Gram-positive organisms. When infection does develop in penetrating wounds, and it should be rare, penicillin-resistant *Staphylococcus aureus* and Gram-negative organisms such as *Escherichia coli* and *Pseudomonas pyocyanea* are commonly found. It follows that meningitis secondary to infection in brain wounds is due to the same organisms.

(*b*) *Prevention*

The first step in prevention consists of avoiding local sepsis in fractures of paranasal sinuses and in penetrating brain wounds. The second step, as outlined previously, consists of administering penicillin, 200,000 units daily for 5

rhinorrhoea accompanies such a lesion, if only for a few days. Should comminution of a frontal sinus be marked, and accompanied by comminution of ethmoidal cells, as is the case in many gunshot wounds involving this region, it may be considered desirable to carry out unilateral or bilateral radical exenteration of frontal sinuses and ethmoids. The dura is then repaired by suture or by fascial grafting and the scalp closed. A drainage tube is brought out through the nose.





Fig. 194.—Multiple comminuted fracture of right frontal region, right frontal sinus and ethmoid cells: postero-anterior and right lateral views. (*By courtesy of the Department of Radiology, Toronto General Hospital.*)

Radical operation

In the treatment of multiple comminuted *fracturing of the frontal sinus* and ethmoids, with or without a penetrating wound involving the fronto-ethmoidal region and the brain (Figs. 193 and 194), the outstanding problem involved is whether it is wiser to wait for a few days, during which the patient receives intensive penicillin and sulphonamide therapy, before turning a bone flap and doing a fascial graft, unilateral or bilateral, or to perform *an immediate primary definitive* operation. This requires radical removal of all damaged soft tissues and bone fragments with exenteration of involved frontal sinus and ethmoidal cells, unilaterally or bilaterally; torn dura is repaired by fascial graft and orbital fascia is incised so that orbital fat bulges up and helps to obliterate the dead space; complete primary closure of the scalp is carried out. In this type of case the author favours primary definitive surgical cleansing with repair of dura, or packing and primary closure, save for nasal drainage.

This group of cases constitutes one of *the most difficult problems of brain* injury, and as in World War II it was found advisable to transfer this type of case from a mobile surgical unit to a base hospital for treatment, so, in civilian life, it is advised that patients should be transferred to the nearest neurosurgical centre.

Risk attendant upon incomplete operation

Following incomplete primary operation, sepsis at the site of injury occurs commonly and may be followed by the intracranial spread of infection; pneumo-cranium may result (Fig. 195). Both these complications are rare following complete primary definitive surgery. A pre-operative delay of 1 to 3 days under intensive penicillin and sulphonamide therapy has been found less dangerous, with regard to sepsis, than incomplete primary operation.

are administered parenterally and 50 milligrams twice daily by lumbar puncture. This regimen has been successfully utilized in a case of meningitis due to *Esch. coli*, following upon fracturing of the paranasal sinuses with incomplete primary operation, brain abscess and pneumo-cranium.

Failure of treatment with penicillin or streptomycin may be due to an adhesive block in the subarachnoid space preventing diffusion of the antibiotic. At each lumbar puncture a manometric examination should be performed with compression of the jugular veins. If a block is present, cisternal or ventricular injection must be carried out.

Treatment of primary septic focus

In the presence of pneumococcal meningitis, fractures involving the paranasal sinuses require surgical treatment when pus is pocketing, when drainage from the sinuses is interfered with, and when a penetrating wound is present. Such treatment is as outlined under the heading of "Fractures involving paranasal sinuses", save that gauze packing should be used in place of fascial grafting and drainage established through the nose. The scalp is completely closed.

Meningitis associated with a linear fracture commonly subsides under chemotherapy alone. At a later date a fascial graft may be considered necessary.

Surgical intervention is rarely required because of persisting otorrhoea. If otorrhoea is present and mastoiditis flares up or develops, a radical mastoid operation is indicated.

The treatment of an unencapsulated, infected brain wound causing meningitis, as evolved in World War II, consists of radical removal of all softened, septic brain and foreign material, and closure of the scalp without drainage. Streptomycin or penicillin, as indicated, is injected into the cerebral defect, as well as into the lumbar subarachnoid space, by a spinal needle.

9. COMPLICATIONS OF BRAIN INJURY—LATE

(1) Chronic subdural haematoma

Often the result of a head injury so trivial as to escape attention, chronic subdural haematoma constitutes a diagnostic problem after a latent interval of weeks or months. Though often difficult to diagnose, surgical treatment in good time produces such excellent restoration of brain function that physician, surgeon and psychiatrist must be ever conscious of the possibility of this lesion.

(a) *Pathology*

Chronic subdural haematoma is a late stage of acute subdural bleeding (Munro and Merritt, 1936). In the majority of instances the chronic haematoma consists of a large collection of dark, fluid blood, with a few fragmentary clots either floating about or adherent to inner or outer membrane. The haematoma originates from haemorrhage and pocketing of cerebrospinal fluid in the subdural space. The haematoma extends over the greater part of the supero-lateral surface of the cerebral hemisphere, being encapsulated by a thin inner membrane which is not adherent to the arachnoid and an outer membrane which thickens and blends with dura with the passage of time. In some 5 per cent of cases the lesion is bilateral.

The solid haematoma is that in which only blood is deposited in the subdural

to 7 days, following injury or the cessation of bleeding or the escape of cerebrospinal fluid from the nose or ears. Sulphadiazine, 3 to 5 grammes, is given on admission and a level of 10 milligrams per cent maintained in the blood for a like period. On this regimen, meningitis in the days following receipt of linear fracture of the frontal sinus is very rare.

(c) Diagnosis

Lumbar puncture

The development of confusion or semi-coma accompanied by rising fever, increasing rigidity of the neck and Kernig's sign requires lumbar puncture and the examination of the cerebrospinal fluid. Turbid or milky fluid under increased pressure with increased total protein and a white-cell count ranging from several hundred to several thousand, predominantly polymorphonuclear leucocytes, establishes the diagnosis. A smear should be stained and examined for bacteria, and the cerebrospinal fluid cultured. It must be noted that post-traumatic meningitis may be accompanied by a rectal temperature of only 101·4°–102° F. On occasion, the mental stupor and confusion leading to coma are so striking as to suggest, on superficial examination, the development of an intracranial clot rather than meningitis.

(d) Treatment

Effects of delay

Early intensive treatment of meningitis is particularly important for, if delay occurs before the infection is controlled, adhesive meningitis may produce serious sequelae. Deafness and tinnitus may result from involvement of the acoustic nerve; an adhesive block of the foramina of Majendie and Luschka results in internal hydrocephalus; obliteration of spinal arteries may result in posterior column degeneration, and so on.

Penicillin

Meningitis due to Gram-positive organisms is treated by the addition of intrathecal penicillin to a regimen of parenteral penicillin and sulphadiazine. A dosage of 20,000 units of crystalline penicillin is administered by lumbar puncture. Administration is slow; an initial dilution of 2,000 units per cubic centimetre is used, and by interchange with cerebrospinal fluid dilution is progressively increased during administration. Intrathecal penicillin should be given without awaiting the results of cultures of cerebrospinal fluid and carried on twice daily by lumbar puncture for 48 hours. If the organism is penicillin sensitive and the subarachnoid space is not being constantly reinfected, substantial improvement in temperature should have occurred, with clearing of cells from the cerebrospinal fluid. Penicillin, with clinical improvement by intrathecal route, may be reduced to 5,000 to 10,000 units once daily until the temperature has been normal for 24 to 48 hours. Parenteral penicillin and sulphadiazine should be carried on for a minimal period of 5 to 7 days after the temperature is normal.

Precautions

Precautions regarding the intrathecal administration of penicillin are most necessary, for cases of transverse myelitis resulting in paraplegia are on record following the rapid injection of highly concentrated impure penicillin. Similarly a fresh ampoule of penicillin should be prepared for each injection, as Gram-negative organisms have been found in penicillin containers used on several occasions and stored between use (Botterell and Magner, 1945).

Streptomycin

Meningitis due to Gram-negative organisms is treated by streptomycin. In using this antibiotic it is extremely important to use massive doses initially, for organisms quickly develop a tolerance to it. One to two grammes per day

(iii) *The third type of clinical picture* includes psychoses, mental incapacity and epilepsy. The formation of a unilateral diffuse solid clot or bilateral frontal clot organizing and, in rare instances, calcifying, may so disrupt the mental and emotional levels of cerebral function that patients are committed to mental hospitals. Operation or necropsy was performed on 4 such cases in Ontario hospitals in a 2-year period.

Papilloedema and local disturbance of cerebral function, in relation to function of cranial nerves, motor-power and reflexes, and sensation, are lacking in such cases.

Pneumo-encephalography and ventriculography

In the absence of calcification of clot, or displacement of a calcified pineal gland shown in x-ray films of the skull, air studies or burr holes may be necessary to establish a diagnosis.

A chronic subdural haematoma, mixed (fluid) or solid, can be excluded only by bilateral burr holes, pneumo-encephalography or ventriculography.

(c) *Surgical treatment*

Bilateral burr holes are made in the mid-temporal region immediately below the upper border of origin of temporal muscle. The presumably unaffected side is explored first and, if negative, the incision is closed.



FIG. 196.—Site of drainage of chronic mixed (fluid) subdural haematoma in right mid-temporal region. Note left parietal burr hole used for ventriculography. (*By courtesy of the Department of Radiology, Toronto General Hospital.*)

Evacuation of haematoma

In the presence of a mixed (fluid) chronic subdural haematoma, as the dura is incised by degrees, a blue membrane presents which is similar to a "blue-domed cyst". The burr hole is enlarged with rongeurs to about 3×3 centimetres (Fig. 196). The dura and outer membrane are incised with knife and grooved director in cruciate fashion and retracted by means of sutures. Dark, bloody fluid and fragmentary clots are evacuated by suction and irrigation. A burr hole may be necessary in the parietal region if through and through irrigation is desired. A bone flap should not be turned down, adding as it does to the risk of a post-operative clot (McKenzie, 1932).

Treatment of deep membrane

Separating the haematoma from brain is a thin semi-transparent "deep" membrane. This is picked up with delicate, toothed forceps, taking care to avoid damaging cortical vessels, incised, and split radially in several directions. It is believed that this facilitates expansion of the compressed brain, lying as it often does an inch or more from the dura. The deep membrane is not adherent to cortex. In adults, removal of the membrane is unnecessary.

Large tube

Temporal muscle and scalp are then closed, in layers, round a rubber tube, approximately $\frac{3}{8}$-inch inside diameter, sutured in place so that it extends only to the plane of the dural opening. The free edge of the aponeurosis of the scalp around the tube is sutured to the scalp $\frac{1}{2}$ an inch from the incision to maintain haemostasis.

During the 24 hours following operation, the patient must receive 3,000 to

Pathology of solid chronic subdural haematoma

space at the time of the acute haemorrhage. Organization of the clot is rapid, and when the clot is not excessively thick only the centre may remain partially liquefied as a result of local necrosis. There is no progressive increase in size of a solid subdural haematoma.

Latent interval; progression in size of mixed (fluid) chronic subdural haematoma

The acute mixed (fluid) subdural haematoma gradually increases in size because the initial fluid mixture of blood and cerebrospinal fluid in the subdural space is of high osmotic pressure and is diluted with additional fluid from the cerebrospinal fluid. The assumption is necessary that the arachnoid acts as a dialysing membrane and that fluid passes through it from cerebrospinal fluid to the subdural mixture of bloody cerebrospinal fluid which is of much higher osmotic pressure. The increase in fluid and decrease in protein content of the subdural haematoma over the first 3 months are supported by the results of the experiments of Gardner (1932).

Solid haematomas

By contrast solid haematomas become progressively more fully organized and eventually calcification may take place.

(*b*) *Diagnosis*

The clinical picture of chronic subdural haematoma may be broadly classified into three main types. (i) *The first, and most frequently encountered surgically*, is essentially that of increasing intracranial pressure, and is due to mixed (fluid) subdural haematoma. Within a few days or weeks of a minor head injury the individual suffers headaches which continue, and increase in severity. Vertigo may become troublesome on change of position. Fits may occur in a small percentage of patients. Periods of mental confusion may develop. Finally, the patient is referred to hospital because of increasing drowsiness, headache and finally coma—the picture of increasing intracranial pressure.

Examination reveals papilloedema in only about half the number of such cases. Visual field defects are rarely, if ever, present. Pupillary changes are uncommon and lateralizing or localizing signs in terms of power, reflexes and sensation are both relatively uncommon and unreliable.

Skiagrams of the skull may show a shift of a calcified pineal gland, thus lateralizing an intracranial space-occupying lesion.

The diagnosis of this type of case depends upon the history, which very often is lacking in information. It is not difficult to appreciate why the diagnosis before operation is often "brain tumour unlocalized", for the history is basically that of increased intracranial pressure.

Burr holes and air studies

The final step in diagnosis is to make bilateral burr holes in the upper midtemporal regions under the temporal muscle. Failure to demonstrate a clot after opening the dura then requires that ventriculography should be done in a search for a cerebral tumour or local mixed (fluid) or solid subdural clot, if the brain is "tight". If there is not evidence of increased intracranial pressure, pneumo-encephalography may be carried out.

(ii) *The second type* of clinical picture in chronic subdural haematoma consists, generally speaking, of local disturbance of brain function due to localized solid clot or mixed (fluid) haematoma. This, typically, produces local disturbance of brain function with cortical sensory deficit, hemiparesis or hemiplegia. Depending upon its size, it may or may not produce headaches and papilloedema due to increased intracranial pressure.

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of writing, an active research programme is under way in the treatment of those casualties of World War II with penetrating brain wounds complicated by epilepsy.

(4) Bone defect of skull

Skull defects resulting from the treatment of penetrating wounds cause concern to the patient and a sense of insecurity, due to fear of injury. The fact that an impulse occurs on coughing and that bulging occurs when the head is dependent are additional sources of worry. In the frontal region a bone defect may be so disfiguring that social and economic rehabilitation are impossible.

It is the writer's view that skull defects, save those deep to temporal muscle, should be repaired as soon after the initial injury as possible, unless the individual patient is quite satisfied to carry on and is pursuing a non-hazardous occupation. There is no convincing evidence that repair of a bone defect either enhances or decreases the likelihood of post-traumatic epilepsy.

(a) Tantalum cranioplasty

Tantalum cranioplasty (Pudenz, 1943) is, in the writer's opinion, the most satisfactory method of repairing skull defects yet put forward. The chief objection to tantalum is that it is radio-opaque and a large plate may seriously reduce the efficiency of future pneumo-encephalography. Against this disadvantage it must be pointed out that tantalum is inert, causing very little tissue reaction, and may be shaped or trimmed at the operating table or before; a tantalum plate does not interfere with electro-encephalography.

Shaping of plate

A variety of special techniques have been put forward to aid in the reproduction in tantalum plates of the contours of the skull. Experience with a method instituted by McCormick (1944) has shown that a skilled sheet-metal worker can, in a few minutes, shape a well-fitting, smooth plate. Given a skull, skiagrams showing the size of the bone defect, and the patient with scalp shaved and sitting erect so that the defect has a concave surface, the Department of Prosthetic Services of Christie Street Hospital, D.V.A., has produced a hundred or more almost uniformly satisfactory plates. It is better to have a plate on the large side than one too small, for the plate may be trimmed with scissors at the operating table.

Operation

The incision in the scalp must be planned to ensure tension-free closure over the plate. The margins of the plate are made to overlap the margins of the bone defect, and the plate either wired in place through drill holes or fixed with tantalum screws. It has not been found necessary to bevel the bony margins of the defect. The plate is perforated to avoid blood or cerebrospinal fluid pocketing deep to it.

(b) Post-operative treatment

Collection of fluid deep to scalp

To minimize the post-operative accumulation of fluid deep to the scalp, complete haemostasis is necessary. This is facilitated by the use of local anaesthesia (1 per cent procaine hydrochloride with adrenaline). A well-padded dressing should be gently but firmly applied and remain undisturbed for 10 days. Drains are not used.

Soft-tissue deficiency

A common error of judgement in the pre-operative assessment of bone defects involving forehead and supra-orbital ridge is to underestimate the amount of skin necessary for tension-free closure following restoration of normal contours of the cranium. The cooperation of plastic surgeons is of

Intravenous fluids: expansion of brain

4,000 cubic centimetres of normal saline intravenously to aid in expansion of compressed brain. At the end of this 24-hour period the patient is returned to the operating room and the brain inspected through the drainage tube. If the brain has expanded fully, the tube is removed and the incision closed. If expansion is incomplete, the large tube is removed and the incision closed round a soft rubber Penrose drain leading into subdural space; this is removed 24 hours later and sutures, previously placed, are tied to close the track. An additional 2,000–3,000 cubic centimetres of normal saline are administered in the second 24 hours.

Recovery of cerebral function is contingent upon expansion of the compressed brain. Operation should be carried out before atrophy of brain has developed as a result of long-continued compression. Expansion of brain following operation should be complete before drainage is discontinued or the subdural haematoma may be replaced by pocketing of cerebrospinal fluid in the subdural space forming a subdural hygroma.

Solid chronic subdural haematoma

Evacuation of a solid chronic subdural haematoma, localized by air studies, or encountered with exploratory burr holes, requires exposure by means of a bone flap as for removal of a brain tumour.

(*d*) *Results*

The mortality rate following evacuation of a mixed (fluid) chronic subdural haematoma is of the order of 5 per cent. A low death rate is dependent upon early diagnosis. The fact that many patients are still admitted comatose or semi-comatose increases risk to life in these cases.

Operation is accompanied by a somewhat higher mortality rate with solid chronic subdural haematoma because of the necessity of a bone flap.

(2) Chronic subdural hygroma

The presence of yellow fluid, high in protein content in the subdural space, originates in pocketing of cerebrospinal fluid in the subdural space. Increase in size over a 3-month period, clinical history and physical findings, and treatment are the same as for a mixed (fluid) chronic subdural haematoma. In fact chronic subdural hygromas are so uncommon that they are almost always labelled chronic subdural haematomas before operation. Exclusion of a chronic subdural hygroma requires burr holes, ventriculography or pneumo-encephalography.

(3) Post-traumatic epilepsy

Epilepsy of focal origin develops in from 35 to 50 per cent of patients who receive penetrating brain wounds. In about half of the cases convulsive seizures begin within the first year, but the onset may be delayed for years. In the absence of a penetrating brain wound, that is in closed head injuries, the incidence of post-traumatic epilepsy is of the order of 1 to 2 per cent.

Treatment

Post-traumatic epilepsy may be controlled by anti-convulsant therapy with phenobarbitone (Phenobarbital, *U.S.P.*) and sodium diphenylhydantoinate (Diphenylhydantoin Sodium, *U.S.P.*; Dilantin) in appropriate dosage. Should seizures occur in spite of an efficient medical regimen, such patients should be investigated at a neurosurgical centre especially set up for and interested in the surgical treatment of epilepsy. By means of electro-encephalographic studies pre-operatively and from the exposed brain, the abnormal discharging focus may be localized and excised with beneficial results. At the time

Cluff (1946) reported 3 infections in 75 consecutive tantalum cranioplasties done at Christie Street Hospital, D.V.A. Necrosis of overlying scalp was responsible for two infections; the third resulted from establishing a communication at operation with a previously damaged frontal sinus which had not been exenterated. *Infection requiring removal of plate*

Damage to the pseudo-dura overlying the penetrating wound of brain must be avoided when the adherent scalp is being freed by sharp dissection. In one instance it was necessary to repair a cerebrospinal fluid leak with a fascial graft and re-insert the plate at a later operation. *Removal of plate due to accumulation of cerebrospinal fluid*

(c) *Time for tantalum cranioplasty*

Tantalum cranioplasty may be carried out, in our experience, at any time if uneventful healing has followed primary closure without drainage of a penetrating cerebral wound, and retained bone fragments are not a feature. A minimal delay of 3 months is desirable if healing has been complicated by sepsis. Penicillin and sulphadiazine are administered post-operatively in all cases either previously septic, or when the defect is in the neighbourhood of a primarily damaged frontal sinus.

Figs. 197 to 200 show the smooth contours of a forehead reconstructed with a large tantalum plate. The scalp is freely movable over the plate.



Fig. 200 —Bone defect of skull; appearance following tantalum cranioplasty.

(5) Rhinorrhoea and pneumo-cranium

Rhinorrhoea, unnoticed at the time of injury, may continue or commence for the first time months, or years, following injury, with the formation of pneumo-cranium. Fracturing may be confined to the ethmoids and fail to show on x-ray films. Massive frontal subdural pneumo-cranium has resulted in admission to mental hospitals because of confusion and faecal and urinary incontinence. Meningitis may develop.

Treatment consists of intradural fascial patching of the fistulous tract into the ethmoidal air cells as described by Taylor (Eden, 1942), or application of the fascial graft extradurally—a more difficult technical procedure. *Treatment*

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FIG. 197.—Skull defect, right frontal region, resulting from penetrating wound with machine-gun bullet.





FIG. 198.—Bone defect of skull, right frontal region: x-ray films, Waters's position and lateral view; note involvement of frontal sinus; this was not opened at operation. (*By courtesy of the Department of Radiology, Christie Street Hospital, D.V.A.*)





FIG. 199.—Bone defect of skull repaired with tantalum; x-ray films show postero-anterior and lateral views. (*By courtesy of the Department of Radiology, Christie Street Hospital, D.V.A.*)

great value, both in assessment and in preventing failures by supplying additional full-thickness skin, by grafting at preliminary operations. Tantalum cranioplasty should be avoided where operation must be carried out through a dermatome graft.

BRAIN—NEUROLOGICAL INVESTIGATION AND SPECIAL TESTS

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[References to other titles are given under Brain—Injuries and Complications in the Index Volume.]

reflexes; (5) sensory impairment; (6) defect of cerebellar function; (7) endocrine disorder from pressure upon the pituitary body or third ventricle. In respect of these symptoms and signs clinical investigation can contribute to the diagnosis of a space-occupying lesion in two ways. First, it can determine the rate of onset and progress; it is characteristic of nearly all such lesions that the onset of symptoms is gradual, and that they are slowly progressive. Secondly, it can localize the lesion; space-occupying lesions are as a rule single, and involve all neighbouring structures irrespective of their function. The degenerative lesions which are liable to be confused with space-occupying lesions are usually multiple, or systemic, the latter involving nerve cells or nerve fibres, or a particular set of one or the other. Thus a complete neurological history and examination are essential for the evaluation of this group of symptoms if such common diseases as cerebral thrombosis, disseminated sclerosis and paralysis agitans are to be distinguished.

Onset and progress

Localization

Differential diagnosis

Progressive failure of vision with optic atrophy may be caused by syphilis, glaucoma, tobacco poisoning, nutritional deficiency, and some hereditary diseases such as Leber's atrophy, but a careful examination of the visual fields together with the history usually makes the distinction easy. The progressive unilateral weakness of the limbs which may be the earliest evidence of paralysis agitans is distinguished by the characteristic striatal rigidity and normal reflexes. Focal symptoms from cerebral thrombosis are very rarely of such gradual onset that the diagnosis from a space-occupying lesion must depend upon special methods of investigation. Progressive weakness or sensory impairment on one side of the body may be caused by a tumour of the spinal cord above the cervical enlargement, but neurological examination should always serve to localize the lesion. The history of pressure upon neighbouring structures by an intracranial aneurysm often includes an episode of subarachnoid haemorrhage.

Optic atrophy

Paralysis agitans

Cerebral thrombosis

Tumour of spinal cord

Intracranial aneurysm

(2) Epilepsy

In a considerable number of cases of cerebral tumour, and in some instances of other space-occupying lesions (abscess, granuloma), epileptic attacks are early and important symptoms. These may be major or minor, generalized or focal, depending upon the situation of the lesion, and probably also upon the capacity of the surrounding cortex to resist and restrict the epileptic discharge. Tumours which press upon or invade the cerebral cortex are especially apt to cause epileptic attacks as an early symptom, but deep-seated tumours, for example those involving the corpus callosum, may also do so. Focal attacks arising from lesions in the neighbourhood of the Rolandic fissure may be motor, sensory or sensori-motor. Lesions of the occipital cortex give an aura of flashing, or coloured lights in the opposite visual field; lesions of the uncinate lobe give a transient abnormal smell or taste often associated with a dreamy state; lesions of the superior temporal gyrus sometimes give an aura of sound, complex or crude. A momentary inability to speak or read may be the focal sign of epilepsy from a lesion of the speech centres. Focal attacks are especially apt to be caused by meningiomas because they so often lie in the neighbourhood of the Rolandic and Sylvian fissures. The slow-growing gliomas (astrocytoma, oligodendroglioma) sometimes cause epileptic attacks,

Focal attacks

Signs and symptoms

1. INTRODUCTION

75.] In this article particular attention is focused on the space-occupying lesions of the brain, because of their prominent position in the neurological surgeon's field of work, and to emphasize the neurological approach to his problems. For instance, it is necessary before operation in a case of compound depressed fracture of the skull to determine the presence and degree of neurological disturbance in order to estimate properly the extent of cerebral damage; again, the diagnosis of cerebral compression by a blood clot depends upon a proper understanding of the changing neurological picture. Head injuries are dealt with elsewhere in this work, and consequently, with the exception of chronic subdural haematoma, those expanding lesions which form part of the acute brain-injury syndrome will not be discussed here. Only when a careful history has been taken, and a thorough examination completed, can such special investigations be chosen as will confirm, check and amplify the clinical diagnosis. The neurological surgeon should finally possess information enabling him to localize the lesion accurately, and to make a shrewd surmise as to its precise pathology; he is then qualified to give an opinion as to the advisability and nature of operation. In certain cases the removability of a tumour may remain in doubt until it is exposed at operation.

2. SCOPE OF INVESTIGATION

Clinical analysis

The clinical analysis of symptoms and signs will often in itself afford evidence of a space-occupying lesion within the skull, and may further indicate the situation of the lesion and provide valuable, sometimes, decisive information as to its pathology. The object of clinical inquiry is to carry investigation up to the point at which it may be judged what special methods of examination may be necessary before it is finally decided whether operative or other treatment should be undertaken. The methods of neurological investigation to be described in this article are those which may be of practical value in approaching this problem.

3. CLASSIFICATION OF SYMPTOMS AND SIGNS IN SPACE-OCCUPYING LESIONS

The symptoms and signs of a space-occupying lesion may be classified for practical purposes as follows.

(1) Symptoms due to loss of function from direct pressure upon structures *in the neighbourhood of the lesion*

These are obviously as many as there are specialized functions at risk. A lesion in one of the more silent areas of the brain may cause symptoms of mental disorder only, providing a diagnostic problem which will be discussed separately. Apart from this the list of possible symptoms is a long one: (1) interference with the functions of speech or with the intellectual processes concerned in perception and recognition (agnosia) or of automatic performance (apraxia); (2) visual defect from pressure upon optic nerves, chiasma, optic radiations or occipital cortex; (3) impairment of smell or hearing or involvement of other cranial nerves; (4) weakness of upper neurone type, involving face, palate, tongue or limbs with appropriate alteration of the

may for a long time cause no symptoms other than those of mental disorder. The commonest sites for such tumours are the frontal lobe, the corpus callosum and the temporal lobes. They are nearly always gliomas.

Differential diagnosis

The complaints of difficulty in concentration and apathy may lead to an erroneous diagnosis of neurosis, but this should be avoided if a careful history is taken, and the ordinary clinical tests of intellectual function are employed. The anxious or depressed patient may have difficulty with these tests owing to preoccupation or retardation, but failure without such reason is characteristic of organic cerebral disease. When it is concluded that the symptoms are those of organic disease, causes other than a space-occupying lesion have to be considered of which the following are of most practical importance. Dementia paralytica can often be detected by abnormalities of the pupils or reflexes, dysarthria or tremor, but in the absence of such signs can only be excluded by examination of the cerebrospinal fluid. Cerebral arteriosclerosis is usually associated with a high blood-pressure, and retinal arteriosclerosis, but in elderly persons these signs may be absent. In the presenile dementias (Alzheimer's disease, Pick's disease) the onset of mental disorder is usually more insidious and the history longer than in cerebral tumour, but in many cases the differential diagnosis can be made only by skiagrams of the air-filled ventricles.

Neurosis

Dementia paralytica

Cerebral arteriosclerosis

Presenile dementias

(4) Symptoms arising from increased intracranial pressure

These are due on the one hand to stretching of pain-sensitive structures, especially the blood-vessels in the neighbourhood of the lesion, and on the other hand to interference with the circulation of the blood and cerebospinal fluid, which together with the bulk of the lesion causes expansion of the intracranial contents. Headache is the most important of these symptoms. It is characteristically intermittent with a tendency to occur in the early mornings, described as aching, throbbing or expansile, and aggravated by coughing, straining, physical effort or stooping, by which it may also be precipitated. Its distribution varies and has no great value except that when it is, from the first, suboccipital it is suggestive of a lesion in the posterior fossa. Severe and persistent bi-temporal headache should arouse the suspicion of a pituitary tumour. Transient sharp headache provoked by sudden change of posture suggests an obstructive hydrocephalus from a lesion involving the Sylvian aqueduct or third or fourth ventricles. Vomiting in association with the headache is an important, but not a constant symptom, and may or may not be attended by nausea. Papilloedema may be an early or a late development, and may occur without any subjective visual disorder. The patient with a space-occupying lesion, with or without papilloedema, often complains of transient dimness of vision on stooping. Diplopia from a sixth nerve paresis is not uncommon. Drowsiness (at first episodic), mental dullness, epileptic attacks, vertigo and tinnitus are other common symptoms of increased pressure.

Headache

Vomiting

Papilloedema

Differential diagnosis

Of the diseases which may simulate the pressure symptoms of a space-occupying lesion, the following are of practical importance. Migraine is a common cause of headache and vomiting. The attacks may be distinguished by the characteristic aura if present, by the long intervals of freedom from

Migraine

generalized or focal, for years before any other symptoms develop. Extradural and subdural haemorrhage rarely cause epilepsy and the same is true of temporal-lobe abscess. A frontal abscess, however, not infrequently declares itself with focal attacks. Space-occupying lesions causing generalized attacks are most often found in the frontal lobes. The attacks may be minor—a brief loss or disturbance of consciousness—or major with generalized convulsive spasm.

All space-occupying lesions causing epileptic attacks sooner or later produce interparoxysmal symptoms, loss of function from local pressure, symptoms of increased intracranial pressure, or impairment of mental function. A space-occupying lesion may also cause epilepsy indirectly through increased intracranial pressure, the attacks being then as a rule generalized.

Differential diagnosis

[Id]iopathic [ep]ilepsy

Apart from space-occupying lesions there are many diseases which may cause epileptic attacks, for example, inflammation, degeneration, congenital defect and vascular lesions, but by far the most common source is that known as idiopathic epilepsy. In about a quarter of the number of cases of idiopathic epilepsy, there is a family history of the liability, and in three-quarters of the number of cases the attacks begin before the age of 20 years. They are nearly always of the generalized type, and if there is a focal aura this tends to become less prominent with repetition of the attacks. It follows, therefore, that focal attacks at any age should arouse the suspicion of an organic cerebral lesion, and that generalized attacks beginning after the age of 20 years in a person with no family history of epilepsy should be equally suspect. The case for or against a space-occupying lesion should be further considered in the light of clinical history and signs. A history of head injury should be especially inquired for and also a history of any infection which might have caused cerebral thrombophlebitis. In young persons birth injury and encephalitis complicating the exanthemata have to be considered. In older persons, syphilis, cysticercosis, cerebral arteriosclerosis and presenile dementia must be taken into account. The commonest cause of epilepsy beginning in an adult with a negative family history is probably a cerebral tumour, and special investigations including electroencephalography, examination of blood and spinal fluid, skiagrams of the skull, and an encephalogram or ventriculogram are often necessary to complete the diagnosis.

[Ce]rebral [tu]mour

(3) Dementia

[Sig]ns and [sy]mptoms

In some cases of cerebral tumour and, more rarely, in cases of cerebral abscess or chronic subdural haematoma, the presenting symptoms are those of mental disorder. Intellectual impairment is usually the first evidence. The patient becomes forgetful especially for recent events, is unable to think with his customary quickness and precision, is easily confused and may be imperfectly oriented for time, place or person. Personality-change as a rule is less evident, but in some cases a deterioration in this respect is the first sign of serious illness. The patient becomes careless, irritable or apathetic. He may wet his bed without any concern, or surprise his relatives by coarseness of speech or manners. Clinical examination may reveal other evidence of the kind described in the previous sections which makes the diagnosis of tumour probable or certain, but tumours involving the more silent areas of the brain

cisterna magna. A manometer should always be employed when diagnostic lumbar puncture is performed in order that the pressure of the fluid may be measured, and in the event of this being high, to prevent an excessive loss which might prove fatal. The flexed patient should be placed in the lateral position with the midline of the skull and spinal column precisely in the same horizontal plane; in this position intracranial pressure is the same as the pressure in the lumbar theca, except in certain cases of marked pressure herniation of the brain producing block at the hiatus tentorii or at the foramen magnum (Smyth and Henderson, 1938); in this event intracranial pressure is higher than that obtained by lumbar puncture. If the patient's head is lower than the lumbar spine a manometer in the theca will register too low a pressure, and conversely too high a pressure if the head is above the spine. An unduly high pressure will also be registered if there is straining, compression of the large veins in the neck or cerebral anoxia. High pressures occur in ether anaesthesia or when there is an excess of carbon dioxide in the blood. Although local anaesthesia is the method of choice for the puncture, a barbiturate anaesthesia with free oxygenation is permissible and at times desirable. *Pressure*

The normal range of intracranial pressure is usually regarded as 100 to 180 millimetres of water, and although the pressure is commonly raised in cases of expanding lesions, this is by no means always the case. *Normal range of pressure*

When an expanding lesion is suspected, and there is raised pressure, not more than 2 cubic centimetres of cerebrospinal fluid should be removed for analysis, for fear of precipitating pressure herniation. The type of manometer employed should be such that the capacity of the system when full should not exceed 2 cubic centimetres; a loss from the cerebrospinal axis of more than this quantity may lower the pressure considerably. The Greenfield manometer registering at 300 millimetres contains only 1 cubic centimetre of fluid. *Manometer*

Queckenstedt's test is sometimes of value, for instance in suspected lateral sinus thrombosis when there may be no rise of pressure in the lumbar theca when the jugular vein on that side is compressed; but a free rise does not exclude thrombosis as this may be only mural, or there may be free communication across the middle line through small sinuses at the base of the skull. *Queckenstedt's test*

Abnormality of the constituents of the fluid may give valuable information for diagnosis, and the reader should consult standard text-books for general information on this subject. Special reference is made here only to those abnormal findings which have particular application in the diagnosis of lesions likely to be encountered by the surgeon. It is important for him to know the normal values of the cell and protein content of the fluid at different levels. In the lateral ventricles the protein should not exceed 10 milligrams per cent and the white cells (lymphocytes) one per cubic millimetre; in the cisterna magna 25 milligrams per cent, and in the lumbar theca 45 milligrams per cent and 3 lymphocytes per cubic millimetre. If the fluid has been contaminated with blood during the puncture, due allowance can be made provided the red blood cells are counted, which should always be done as a routine; for every 1,000 red cells there will be an approximate increase of 1·5 milligrams of protein per cent and 2 polymorphonuclear cells per cubic millimetre. No significance should be attached to the presence of a few polymorphonuclear cells (which may be important) unless the red blood cells have also been counted. *Abnormal findings*

headache, and as a rule a family history of the complaint. Headache, vomiting, drowsiness and papilloedema may be observed in patients with malignant arterial hypertension. The raised blood-pressure—the diastolic pressure being usually about 120—a high blood urea, and retinal arteriosclerosis serve to distinguish these cases. Hydrocephalus resulting from chronic inflammation at the base of the brain may cause all the pressure symptoms which have been described. The causes to be looked for are a recent history of meningitis, or evidence of syphilitic infection. Cerebral thrombophlebitis will also cause symptoms of increased intracranial pressure from obstruction of the superior longitudinal or lateral sinuses. The onset of symptoms following otitis media or sinusitis, in the puerperium, or in association with phlebitis in other parts of the body is a clue to diagnosis.

Arterial hypertension

Hydrocephalus

Cerebral thrombophlebitis

4. CLINICAL INVESTIGATION AS AN AID TO PATHOLOGICAL DIAGNOSIS

Although about 90 per cent of space-occupying lesions within the skull prove to be tumours, those of traumatic or inflammatory origin are important because they are usually more amenable to treatment, and are often recognizable if the history is properly taken. A story of head injury should always be asked for with allowance for the fact that what appears to have been a minor injury may be the origin of a subdural haematoma, and that there may be a delay of some weeks between the accident and the beginning of symptoms. It is equally important to inquire for a history of otitis media, sinusitis or local infection of the scalp, or a chronic abscess from one of these sources will sooner or later be missed. An intracranial tuberculoma should be suspected in young people with a history of this infection. The possibility of a parasitic granuloma will be especially considered if the patient has lived in India (cysticercus), Northern China (*Schistosoma japonicum*) or Australia (hydatid). If the diagnosis of tumour is made, clinical observation will often go far towards establishing its nature. In middle-aged and elderly patients examination will sometimes discover a primary growth elsewhere. Palpation of the skull may reveal local thickening highly suggestive of a meningioma, or auscultation a bruit characteristic of an arterial angioma. Certain tumours again have situations, rates of growth and age incidence which in combination have considerable value in pathological diagnosis—for example the rapidly growing glioblastoma of the cerebral hemisphere in elderly persons, the pituitary adenoma and the acoustic tumour—in which special methods of investigation are necessary only to confirm clinical deduction.

Clinical observation

It is to be recognized that a high proportion of supratentorial tumours are undifferentiated rapidly growing gliomas (glioblastomas) which are not amenable to surgery. When such a tumour is suspected on clinical grounds, and it has been accurately localized either by clinical examination or by one of the special methods of investigation to be described, biopsy is the only sure way of establishing the pathological diagnosis.

Biopsy

5. SPECIAL INVESTIGATIONS

(1) Cerebrospinal fluid

A sample of cerebrospinal fluid is usually obtained by lumbar puncture, although on occasion it may be necessary to puncture a lateral ventricle or the



Fig. 201 (*a*).—Skull—normal adult. Lateral projection.



Fig. 201 (*b*).—Postero-anterior projection.



Fig. 201 (*c*).—Antero-posterior projection, tube tilted 35° towards vertex. The dorsum sellae (*a*) is seen through foramen magnum, and the internal auditory meatus (*b*) and the anterior clinoid process (*c*) are well defined on the right side.

(a) Brain tumours

Gliomas

The majority of gliomas do not give rise to changes in the cerebrospinal fluid although an increase of protein is fairly common. This may occur in the ventricular fluid in a deeply seated or basal ganglia tumour, and comparison of the fluid from each ventricle may indicate which side is involved. In brain-stem and posterior fossa tumours the ventricular fluid is normal, although the cisternal and lumbar fluids may contain increased protein. A moderate pleocytosis (up to 100, rarely, considerably higher) mainly mononuclear, but sometimes predominantly polymorphonuclear, with an increase of protein (50 to 100 milligrams per cent) in a fluid which may be xanthochromic suggests the presence of a necrotic tumour near the lateral ventricle. It is important to note that polymorphonuclear cells may be present in expanding lesions other than abscess. In children, a cerebellar medulloblastoma may give rise to similar changes, and because this form of tumour tends to disseminate throughout the cerebrospinal spaces occasionally tumour cells are found. A meningioma, especially if it is arising from the skull base, frequently gives rise to an increase of protein (50 to 150 milligrams per cent) in the fluid, and a high protein content (100 to 400 milligrams per cent) is almost invariably present in cases of acoustic neurofibroma.

Necrotic tumour

(b) Brain abscess

The changes in the cerebrospinal fluid vary considerably according to the mode of invasion of the brain, and the degree of meningeal response. Where infection spreads from an acute frontal sinusitis or an acute mastoiditis, all the stages from a localized suppurative encephalitis to a mature and walled-off abscess are reflected in the fluid. At first there may be a frankly purulent fluid with polymorphonuclear cells predominant, and with the protein raised to several hundreds of milligrams per cent, but without organisms, and with sugar still present and with normal chloride content. Subsequently, the cell count falls and becomes lymphocytic, while the protein for a time remains high. If organisms are found in a frankly purulent fluid with diminution of chlorides (550–700 milligrams per cent) and absence of glucose, generalizing suppurative meningitis is present, and analysis gives no aid in detecting an abscess. In a chronic or slowly developing abscess (such as secondary to pulmonary suppuration) the only abnormality may be slight excess of lymphocytes and a moderate rise of protein (50–100 milligrams per cent). Rarely, a cerebral abscess may cause no abnormality in the cerebrospinal fluid, but a normal cerebrospinal fluid practically excludes an abscess in the cerebellum. Thus the changes vary considerably in cases of brain abscess, but the most significant findings are a persistent high protein even though the cell count is not much raised, and in cases with a cloudy or purulent fluid the absence of organisms with normal chloride and glucose content.

Purulent fluid

High protein content

(c) Subdural abscess

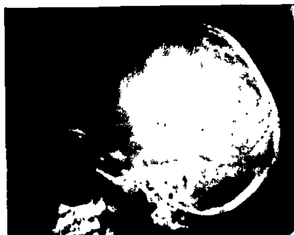
If this is unassociated with thrombophlebitis of the dural venous sinuses the cerebrospinal fluid is usually normal, adding to the difficulties of diagnosis in this dangerous condition.

(d) Extradural abscess

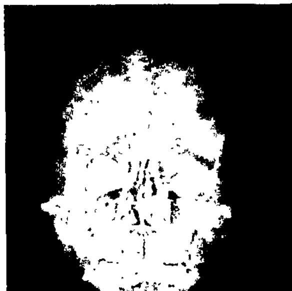
An extradural abscess may be associated with a normal cerebrospinal fluid, but more commonly there is a slight to moderate increase of cells

orbito-meatal plane and 2 centimetres in front of the external auditory meatus; antero-posterior, the orbito-meatal plane being perpendicular to the film, and the tube tilted 35 degrees towards the vertex centring in the sagittal plane, a satisfactory exposure showing the dorsum sellae and anterior and posterior clinoid processes projected within the foramen magnum, the petrous bones and the pineal shadow, if present; postero-anterior projection with nose and forehead on the film, the tube tilted 20 degrees towards the vertex the central ray passing through the sagittal plane, this film giving good definition of the anterior fossa, orbits and lesser wings of the sphenoid, the upper edge of the petrous bones being projected at or below the inferior orbital margins. Stereoscopic films are often of great assistance, and according to the needs of the particular case further special films may be necessary such as skiagrams of each optic canal, a submento-vertical view to demonstrate the base of the skull, or a tangential view to identify thickening of the calvarium or a depressed fracture. Details of these projections are to be found in text-books dealing with these subjects.

Stereoscopic films



(*a*)



(*b*)

Fig. 204 (a), (b).—Separation of sutures, enlargement of sella turcica, rarefaction of posterior clinoid processes, and (for a child) slight increase of convolutional markings. (Cerebellar medulloblastoma in child aged 9 years.)

(*b*) *Fractures*

Postponement of radiographic examination

In closed injuries of the head an x-ray examination need not be regarded as an urgent matter, and apart from certain exceptions should be postponed until the patient can co-operate fully; poor-quality films are worse than useless for they may be misleading. When a depressed fracture is suspected, this should be decided radiographically as soon as possible; stereoscopic and

(lymphocytes and polymorphonuclears) with a normal amount or only slight increase of protein. The chlorides and sugar are unaffected.

(*e*) *Dural sinus thrombosis and cortical venous thrombosis*

Variable findings

The findings in these conditions vary. The fluid may be entirely normal or there may be a mild pleocytosis and slight rise in protein. Changes of this nature may also be due to a brain abscess and the diagnosis frequently receives little help from analysis of the fluid, but an excessive rise of protein favours abscess. These lesions give rise to considerable venous stasis, and even petechial and massive haemorrhages in the brain, and consequently red cells in the fluid favour thrombosis.

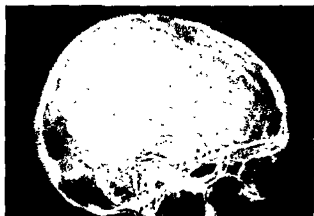


FIG. 202.—Increased convolutional markings in adult skull; note also sharpening of anterior and blunting of posterior clinoid processes. (Case of left acoustic neurofibroma.)

(*f*) *Brain injury*

Useful information can be derived from the cerebrospinal fluid in cases of head injury. It is very desirable to measure the pressure in order to determine whether or not to lower the intracranial pressure. Blood in the fluid indicates that the brain has been severely contused, and if the blood admixture is heavy, laceration of the brain has probably occurred. In cases of subdural haematoma the fluid is frequently faintly yellow and may contain a few red cells and a slightly raised protein, but is often quite normal.

Blood in fluid



FIG. 203.—Enlargement of sella turcica, thinning of anterior clinoid processes and disappearance of dorsum sellae and posterior clinoid processes, the result solely of raised intracranial pressure. Arrow indicates calcification in pineal gland. (Case of left occipital meningioma.)

(2) Radiographic examination

(*a*) *The skull and its contents*

Important information concerning pathological processes affecting the skull and its contents can be detected by x-ray examination, but this depends entirely upon first-class definition, and the choice of appropriate projections (Figs. 201 (a), (b), (c)). For routine purposes four films are advisable: each lateral in which the central ray passes through a point 2 centimetres above the

Projections

turcica may become moderately enlarged (Fig. 203), and there may be thinning and absorption of the lesser wings of the sphenoid (Fig. 205). The cranial emissary veins may increase in size, notably those in the region of the torcular Herophili (Fig. 206).

(d) Focal erosion of bone

Pituitary adenoma

A pituitary adenoma produces the most typical and advanced degree of this radiographic abnormality, owing to the considerable extent to which the tumour is confined within bony walls. The sella turcica becomes greatly enlarged and ballooned in all its diameters (Figs. 207 and 209). The floor gradually sinks until either it is perforated or it reaches the plane of the floor of the middle fossa; the anterior wall encroaches on the sphenoidal air sinus and may completely obliterate it, while the anterior clinoid processes become undermined so that they appear elongated; they may sometimes be sharpened and elevated, probably due to traction on the inter-clinoid ligament by the bulging upwards of the diaphragma sellae. The dorsum sellae is thinned and often displaced backwards, the posterior clinoid processes being eroded. The optic foramina and the superior orbital fissures may be enlarged (Figs. 208 and 210). Although raised intracranial pressure from a slowly growing tumour or hydrocephalic lesion may cause enlargement of the sella, this enlargement rarely reaches the degree resulting from an intrasellar tumour. Moreover, it should be possible to detect the other changes resulting from raised intracranial pressure.



Fig. 207.—Great enlargement of sella turcica—undercutting of anterior clinoid processes, encroachment upon sphenoidal air-sinus; acromegalic features—thickening of vault, massive superciliary ridges, prognathism. (Case of chromophobe adenoma of pituitary gland with fugitive acromegaly.)

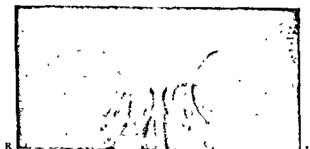


Fig. 208.—Enlargement of the left superior orbital fissure. (Same case as in Fig. 207.)

Other tumours

Focal erosion of bone is produced by other tumours. A slowly growing superficial cerebral glioma may cause thinning and bulging of the overlying calvarium. Occasionally a meningioma may erode both tables to form an

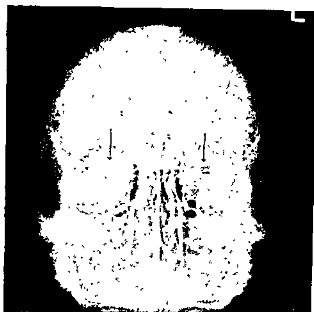


FIG. 205.—Rarefaction of lesser wings of sphenoid. (Case of right frontal astrocytoma. The fleck in left orbit is an artefact.) Compare with Fig. 201 (b).

tangential views may be necessary. In the case of a suspected extradural haemorrhage the radiographic demonstration of a fracture crossing the channel of a dural sinus or a meningeal vessel would be additional evidence in favour. When an operation is to be undertaken for a compound fracture of the skull good films should always be available for the information of the surgeon. They will demonstrate the extent of injury to the bone, the number and situation of the fragments and the presence or absence of opaque foreign bodies. Cerebrospinal rhinorrhoea and acute suppurative meningitis are particularly liable to follow fractures of the anterior fossa which also involve the paranasal air sinuses. Careful technique is necessary to demonstrate these fractures, and good films should be available to aid the surgeon in his decision whether or not operation is advisable.

(*c*) *Space-occupying lesions*

Increased intracranial pressure acting over a sufficient period of time produces characteristic changes in the skull. The convolutional impressions on the inner table, normal in the child but almost absent in the adult, become emphasized (Fig. 202). In children the sutures gradually separate and the head gets bigger (Figs. 204 (a), (b) and 219). One of the most constant and early changes of raised intracranial pressure is absorption of the dorsum sellae and of the posterior clinoid processes. In addition, in long-standing cases the sella

Convolutional impressions

Absorption of bone



FIG. 206.—Enlarged emissary veins at torcular Herophili, the result of raised intracranial pressure. (Case of right acoustic neurofibroma.)

the skull thus giving rise to an external mass. Common sites for hyperostosis are the floor of the anterior fossa, especially the lesser wing of the sphenoid, and the convexity of the skull; in the first named there is sometimes considerable increased bone formation in the temporal fossa and posterior and lateral orbital walls causing proptosis. A hyperostosis is not uncommonly mistaken for an osteoma (Fig. 214), which, however, is usually denser than the surrounding bone. Moreover, an osteoma has a smooth surface, a clear-cut definition and no increase in vascular markings.

Sites for hyperostosis



FIG. 211.—Thinning and elevation of lesser wing of sphenoid, thinning of great wing of sphenoid (postero-lateral wall of orbit) and of lateral wall of middle fossa, due to large meningioma with hyperostosis (arrow) arising from floor of right middle fossa.

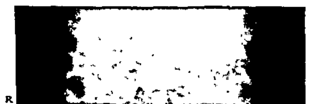


FIG. 212.—Erosion of left internal auditory meatus due to acoustic neurofibroma.

(f) *Abnormal vascular markings in the skull*

In the normal skull the channels lodging the meningeal vessels can usually be detected, branching upwards and backwards from the outer end of the sphenoidal ridge. The diploic vessels vary considerably in degree; commonly, aggregations form irregular spidery star-like patterns in the frontal and parietal regions. The channels are beaded, irregular in calibre and branch and fuse freely; they do not usually transgress suture lines. Increased vascularity of the skull is a common finding in cases of meningioma, the character of the changes being fairly constant and a reliable help in diagnosis (Fig. 215). The bone at the site of

Normal vessels

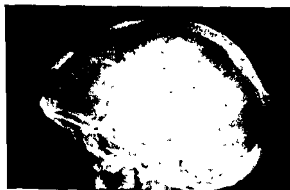


FIG. 213.—Bilateral large diploic channels, well-marked "pitting" for Pacchionian granulations; of no pathological significance.

Increased vascularity

external mass of tumour. Parasellar tumours such as meningiomas may cause destruction of the clinoid processes and the dorsum sellae, on one side only, detectable by a stereoscopic oblique lateral view, and by an antero-posterior film with tube tilted 25–35 degrees towards the vertex; an infra-clinoid aneurysm of the internal carotid artery, if large enough, gives rise to a characteristic erosion causing enlargement of the superior orbital fissure, and of the lateral boundary of the optic foramen; an acoustic neurofibroma commonly causes enlargement of the internal porus acusticus (Fig. 212); in a submento-vertical projection invasion of the base of the skull by a malignant nasopharyngeal growth can sometimes be detected. It is important not to confuse focal erosion of bone with the pits and local impressions seen in the vault, which lodge Pacchionian granulations and lateral lacunae of the sagittal sinus (Fig. 213). These are commonly near the midline, and have a clean-cut margin and dense inner table.



FIG. 209.—Moderate enlargement of sella turcica; slight undercutting of anterior clinoid processes with sharpening; sphenoidal air sinus, dorsum and floor of sella still evident. (Case of chromophobe adenoma of pituitary gland.)

(*e*) *New bone formation*

Meningioma

A meningioma commonly gives rise to the formation of a hyperostosis at the site of its dural attachment (Fig. 211). Its density varies, but its texture is "woolly" compared with the surrounding normal bone and has a rough, sometimes spiculed surface, often pitted by small perforating vessels. The bone surrounding this area is usually marked by many converging fine vessels, and the hyperostosis may on occasion affect the outer as well as the inner table of

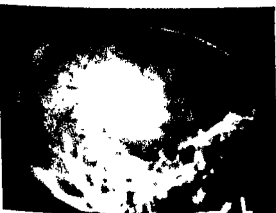




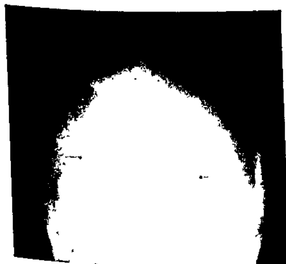
FIG. 210.—Enlargement of the right optic foramen. (Same case as in Fig. 209.)



[illegible]



(a)



(b)

Fig. 217 (a), (b).—Choroid plexus calcification, that on the left side is lower than the right. (Case of left parasagittal fronto-parietal meningioma; verified.)

the dural attachment of the tumour shows loss of texture with pitting of its surface and a local mesh-work of fine vessels. If the tumour is in the vicinity of the meningeal vessels the grooves for these vessels become enlarged, and finer channels may be seen branching towards the site of the tumour. At times there may be enlargement of diploic channels which become broad, smooth and sinuous, converging on the affected area. Occasionally, more distant channels enlarge and may even extend from vault to base. In order to identify these changes it is necessary to compare both lateral projections of the skull, so as to ascertain on which side they occur and whether or not they are bilateral. When diploic channels are large on both sides undue significance should not be attached to them, owing to their wide variation in size in healthy subjects (Fig. 213).

Diploic channels



FIG. 214.—Osteoma of frontal sinus.

(g) *Calcareous deposits*

Calcified plaques in falx

These may or may not be pathological. Calcified plaques arise in the falx in healthy individuals, and are usually best seen in the postero-anterior film, lying in the sagittal plane and taking the form of an irregular dense line or of tent-like projections (Fig. 216). It may be difficult to detect them in the lateral film as they are usually very thin. In about 50 per cent of all skulls normal pineal calcification can be detected; the opacity may be barely visible as a finely granular shadow or may form an irregular or round mass up to 1 centimetre in size in the middle line just above and behind the shadow of the petrous bones (Fig. 203). Considerable enlargement suggests the possibility of a pineal tumour which, however, usually gives rise to a fairly constant clinical picture although ventriculography may be advisable for confirmation.

Pineal calcification



FIG. 215.—Increased vascularity due to a meningioma; the approximate extent of its dural attachment is indicated by arrows.

irregular, wavy, parallel lines.



Fig. 220.—Suprasellar calcification; erosion of anterior clinoid processes, saucer-shaped sella turcica with absence of dorsum. (Rathke-pouch tumour in adult.)

(3) Ventriculography and encephalography

Successful extirpation of intracranial tumours with a low mortality rate demands a high degree of accuracy in localization in order that the craniotomy may be placed to give the best access. Clinical investigation alone may sometimes provide such accurate localization, but frequently more precise information is necessary and, indeed, clinical localization may at times be quite impossible. Since the method was introduced by Dandy in 1918, visualization of the cerebral ventricles and subarachnoid spaces by a gas has become one of the most valued ancillary methods in neurological surgery. It can give information to be obtained by no other method, but unless its limitations and its dangers are fully appreciated the effect on the patient may be disastrous. Air is the contrast-medium usually employed though oxygen is preferred by some, as it is absorbed more readily and is said to give rise to less reaction. In ventriculography the gas is introduced direct into the lateral ventricles by means of a needle inserted through a suitably placed hole in the skull. As a rule only the ventricular system can be seen. Encephalography, by common consent, implies the insufflation of gas by lumbar or cisternal puncture, and not only the ventricles but also the subarachnoid spaces can be demonstrated. Each method has its particular applications, advantages and dangers. Ventriculography is the method of choice when an expanding lesion is suspected. On the other hand, in cases in which cerebral atrophy, arteriosclerosis and epilepsy have to be differentiated from a space-occupying lesion, and there are no

Contrast-medium

Indications

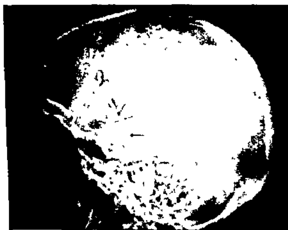


Fig. 221.—Calcification in the wall of an aneurysm of the anterior cerebral artery. An exploratory craniotomy has been performed; the metallic foreign bodies are haemostatic silver clips.

A laterally situated space-occupying lesion may displace the pineal shadow to one side; displacement in the sagittal plane may occur but the information has only limited value. Calcification may also be seen in the glomus of the

Choroid plexus



FIG. 218.—Calcification in a left parietal oligodendroglioma; an encephalogram has been performed.

choroid plexus of the lateral ventricle and the condition is commonly bilateral (Fig. 217 (a), (b)). The normal situations should be recognized so that such shadows are not confused with a pathological opacity; in the lateral view the shadows are seen above and behind the pineal, and in the postero-anterior view they are found above the orbits equidistant from the midline.

Gliomas

Flocculent, streaky and granular types of calcification occur in slowly growing gliomas, more especially the astrocytoma and the oligodendroglioma (Fig. 218). The deposit varies in degree from a small shadow difficult to define to an extensive irregular area sometimes outlining what proves to be a cyst.

Tuberculoma

A healed tuberculoma may calcify and the shadow is more compact and dense than that from a glioma; it is usually small with a crenated edge and may be multiple. Very rarely,

Meningioma and other lesions

calcareous deposits occur in a meningioma quite distinct from the hyperostosis which forms in its base. Calcification occurs in the majority of Rathke-pouch tumours (*synonyms*—suprasellar cyst, adamantinoma), the deposit varying considerably in density and extent (Figs. 219 and 220). It is situated in the middle line just above or sometimes within the sella turcica, and the sella itself is often malformed but it may become ballooned or eroded. Calcification in the wall of an aneurysm of the internal carotid (Fig. 221) forms a clean-cut line with such a curve as to form part of a circle, and in the lateral film may be close to the shadow of the sella turcica, but if it is visible in the postero-anterior view it is seen to be on one side of the middle line. Calcification in an angiomatous malformation usually takes the form of



FIG. 219.—Intrasellar calcification; slight separation of sutures. (Rathke-pouch tumour in a child aged 7 years.)

that the air, which by now is usually under considerably increased tension, can escape.

(ii) *Indications.*—(1) The detection and localization of expanding lesions such as tumours, abscesses and haemorrhages.

(2) The determination of the extent of a tumour, for example frontal glioma extending into corpus callosum.

(3) The demonstration of hydrocephalus and the detection of the site of obstruction.

(4) Failure to perform encephalography.

(iii) *Dangers.*—(1) When an expanding lesion exists there is usually a severe reactionary rise of intracranial pressure within an hour or so; to avoid this the ventricles should be tapped to allow air to escape and operation should immediately follow the procedure. Consequently, ventriculography should only be undertaken by one suitably trained and with facilities to operate, and ventriculography and operation should be considered as two parts of one procedure.

(2) Haemorrhage into or around a tumour.

(3) Haemorrhage into the needle track.

(4) Subdural haemorrhage in gross hydrocephalus.

(5) Hypothalamic crisis in hydrocephalus.

(*b*) *Encephalography*

(i) *Technique.*—This usually gives rise to considerable headache and frequently vomiting, pallor, sweating and disturbances of the pulse rate. Premedication should be heavier than for ventriculography; light narcosis is employed as a routine in some clinics and is always necessary for children. The patient is seated with the trunk, neck and head slightly bent forward in such a position that the eyes are directed towards a point on the floor some two yards ahead. The head, neck and spine must be maintained strictly in the sagittal plane. In the absence of an obstructive or an expanding lesion failure to fill the ventricles is practically always due to faulty position. Lumbar puncture is performed, and the fluid is very slowly replaced by air, with a 10-cubic-centimetre Record syringe. When 20 cubic centimetres of air have been introduced the stilette should be replaced, the head put erect and a postero-anterior film exposed. This will demonstrate whether the ventricles are filling satisfactorily, and if not the position of the patient should be checked. In cases in which the ventricles are seen to be approximately normal in size this amount of air replacement is sufficient to obtain useful pictures, and fractional encephalography of this degree causes only limited discomfort. Total replacement of the fluid is necessary for full visualization of the ventricles and subarachnoid spaces. Better definition is obtained by injecting slightly more air than fluid removed, so as to maintain intracranial pressure, air being so much more compressible than the medium it is replacing. When the lumbar puncture needle has been removed the necessary x-ray exposures are made in the erect and in the recumbent position according to the needs of the case. Air replacement by cisternal puncture is performed in a similar manner, being preferred by some surgeons as it gives rise to less headache; if the ventricles only are to be examined the definition may be better as less air escapes into the subarachnoid spaces. Against these advantages must be weighed the

Premedication

Position of patient

Lumbar puncture

Replacement of fluid

Cisterna puncture

symptoms of increased intracranial pressure, encephalography should be employed.

(*a*) *Ventriculography*

(i) *Technique.*—A pre-operative sedative having been given, the patient is placed supine with the head raised on a sand-bag. The scalp is shaved, cleansed and infiltrated with a local anaesthetic and towels are suitably applied, so that a vertical incision can be made on each side about 2·5 centimetres from the middle line and centred 7–8 centimetres above the external occipital protuberance. The position is not a precise one but the incisions must be symmetrical and placed so that the needle will avoid the sensorimotor and the visual cortical areas. Small self-retaining retractors are inserted and opened, the pericranium pushed aside and holes made in the skull with a Hudson brace and perforator, opening up if it is desired with a burr, though with practice this latter can be eliminated. The dura mater is lifted and made tense by a sharp dural hook and nicked with a tenotome, care being taken to avoid any dural or cortical vessels. A blunt-ended brain needle with a lateral eye is introduced through the brain in a downward and forward direction perpendicular to the skull at that point and parallel to the sagittal plane. Slight resistance can generally be detected immediately prior to entering the ventricle which usually occurs at a depth of about 5–6 centimetres from the dura mater; the stilette is then removed to allow cerebrospinal fluid to appear and a manometer is immediately connected for a pressure reading to be taken. If a hemisphere tumour is present the ventricle on that side may be difficult to locate owing to its displacement or compression. If the first attempt fails the needle should be withdrawn (with the stilette removed in case the ventricle has been completely traversed) and it should be reinserted in a different direction; the direction of the needle should, of course, never be altered while it is in the brain. When both needles are in position fluid is allowed to escape slowly, being replaced by small quantities of air injected gently from a 10-cubic-centimetre syringe. The fluid should be collected and measured, for the quantity indicates the size of each lateral ventricle. It is usual to replace all the fluid by air provided the ventricles are not greatly enlarged, in which case the lowering of intracranial pressure is liable to provoke a serious reaction. Indeed, if marked hydrocephalus is present total replacement may allow the thinned cortex to fall away from the skull, tearing veins and producing a diffuse subdural haemorrhage. A total of 100 cubic centimetres of air may be regarded as a safe maximum. On the other hand, less than 15–20 cubic centimetres of air injected into each lateral ventricle is unlikely to give satisfactory pictures. On occasion, only one ventricle can be tapped and then the head should be turned on that side so as to encourage the passage of air to the other ventricle. If blood issues from the needle when in the brain—the result of tearing a vessel, the needle should be held steady in that position with its stilette removed until the bleeding stops; this diminishes the risk of an intracerebral haematoma. The wounds are sutured and a collodion dressing applied. During the patient's transportation to the x-ray table, great care should be taken that the head is kept slightly raised and in the sagittal plane in order to prevent escape of the air from the ventricles into the subarachnoid space. After the necessary x-ray films have been exposed, it is advisable in those cases in which there is raised pressure to tap a ventricle so

Incisions

Brain needle

Injection of air

Position of head

that the air, which by now is usually under considerably increased tension, can escape.

(ii) *Indications.*—(1) The detection and localization of expanding lesions such as tumours, abscesses and haemorrhages.

(2) The determination of the extent of a tumour, for example frontal glioma extending into corpus callosum.

(3) The demonstration of hydrocephalus and the detection of the site of obstruction.

(4) Failure to perform encephalography.

(iii) *Dangers.*—(1) When an expanding lesion exists there is usually a severe reactionary rise of intracranial pressure within an hour or so; to avoid this the ventricles should be tapped to allow air to escape and operation should immediately follow the procedure. Consequently, ventriculography should only be undertaken by one suitably trained and with facilities to operate, and ventriculography and operation should be considered as two parts of one procedure.

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(3) Haemorrhage into the needle track.

(4) Subdural haemorrhage in gross hydrocephalus.

(5) Hypothalamic crisis in hydrocephalus.

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increased risk of cisternal puncture as compared with lumbar puncture, the need for a co-operative and immobile patient, and the inadvisability of moving the head in order to correct position.

(ii) *Indications.*—(1) To exclude the presence of an expanding lesion in cases in which there is no evidence of raised intracranial pressure.

(2) The investigation of epilepsy due to conditions such as cortical atrophy and porencephaly.

(3) Post-traumatic sequelae.

(4) Organic dementias.

(iii) *Dangers.*—(1) Reactionary rise of intracranial pressure if a tumour is present.

(2) Aggravation or precipitation of temporal lobe or cerebellar tonsil herniation (for these two reasons, if the weight of clinical evidence is in favour of a tumour, ventriculography is the method of choice).

(3) Haemorrhage from an unsuspected vascular malformation.

(4) Precipitation of an epileptiform seizure.

Provided cases for encephalography are carefully selected the risk to life is exceedingly small.

(c) *Projections*

These should be selected with care in each case, and made in the appropriate order, so that maximal information regarding the lesion can be obtained with a minimum of exposures. The air rises to the highest part of the ventricular system, and the position of the film and of the head must be chosen accordingly. *Routine films* The first two films are routine: an antero-posterior in the brow-up position, and a lateral with the patient still supine but with the head slightly extended, thus encouraging the air to enter the third ventricle. If sufficient air has been injected, the films should show the anterior parts of the lateral and the third ventricles. If there is displacement to one side, indicating a lesion of the hemisphere, the patient is turned prone, and a lateral film with the affected side uppermost should demonstrate the ventricle, and a postero-anterior view (occiput up) should show the vestibule, posterior horn and usually the temporal horn of each ventricle. In the event of there being symmetrical dilatation of the ventricles without displacement, the second routine film will demonstrate whether there is any tumour in the anterior part of the third ventricle; if not the obstruction must be sought more posteriorly, and a lateral view should be taken with the patient supine, the neck fully extended and the trunk raised so that the vertex is pointing to the ground. Reid's base line is horizontal in this position. Air should pass into the posterior part of the third ventricle, the iter and the fourth ventricle. The patient is then turned prone for a postero-anterior film with the tube tilted 25 degrees towards the feet, and another lateral view taken with the head flexed as much as possible. In encephalography it is often useful to take postero-anterior and lateral views while the patient is erect so that the highest portion of the lateral ventricles is clearly depicted. Other views are described in works of reference.

(d) *Interpretation*

The interpretation of ventriculograms depends upon a knowledge of the healthy norm (Fig. 222), and an experience of the displacement and deformities produced by lesions in different parts of the brain. The characteristic

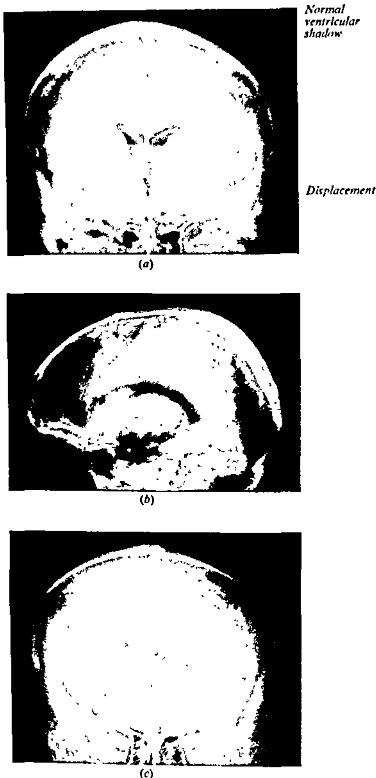
Normal ventricular shadow

shape of the normal ventricular shadow, and its varying density in different parts are precisely related to anatomical boundaries. Comparison of the different projections enable a three-dimensional mental image to be built up (Figs. 223 and 224).

Displacement

Hemisphere tumours cause displacement of the ventricular system to the opposite side, maximal in the area of the tumour; as a rule there is a narrowing of the homolateral and a dilatation of the contralateral ventricle. If the displacement is marked the homolateral ventricle is squeezed under the falx causing an additional displacement in a downward direction affecting mainly the frontal horn and the body, for in the occipital region the great width of the falx prevents displacement across the middle line to any extent. The third ventricle and the septum lucidum are also displaced laterally, and to a degree which varies with the site of the tumour.

Tumours situated deeply in the white matter may bulge into the ventricle, and give rise to a more localized ventricular deformity than a superficial lesion such as a meningioma or a subdural haematoma. Lesions near the midline, such as basal ganglia tumours, produce bilateral hydrocephalus



(*a*)

(*b*)

(*c*)

FIG. 222.—Normal encephalogram. (*a*) A-P. projection, supine. (*b*) Lateral projection, recumbent. (*c*) P-A. projection, prone.

greater on one side; tumours or other obstructive lesions in the third ventricle, iter and posterior fossa produce severe symmetrical dilatation of the lateral

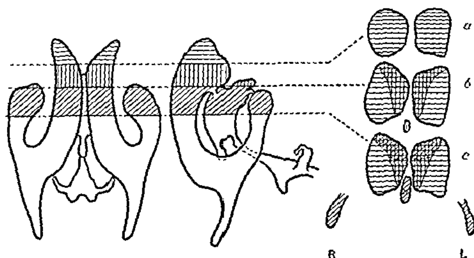


FIG. 223.—Scheme to explain the derivation of the various shadows seen in the A-P. projection (supine) of the air-filled ventricles. Diagrams *a*, *b*, *c* indicate the shadows which would be produced by quantities of air filling the ventricles to three different levels.

ventricles. Examples are given of the common abnormalities, the captions indicating the important points of distinction (Figs. 225–231).

(4) Cerebral angiography

This procedure, introduced by Moniz in 1927, demonstrates the displacement produced in the larger cerebral blood-vessels by tumours and similar

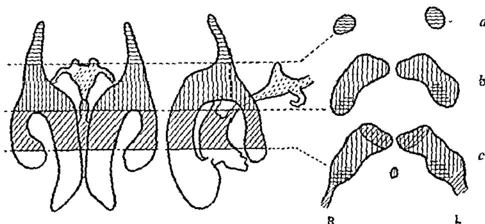


FIG. 224.—Scheme with ventricles in the prone position for P-A. projection. Most of the air has escaped from the third ventricle; this frequently happens in the prone position if there is no obstructional lesion caudal to the third ventricle. The occipital horns normally vary considerably in their shape and size.

l serial rams

lesions, and abnormalities of vessels and of circulation (Figs. 232–235). Rapid serial skiagrams will trace the passage of the opaque medium through the arteries, the capillaries, the veins and dural sinuses, but to do this special



FIG. 225 (*a*).—A-P. projection, supine: anterior part of lateral ventricles displaced to the right, with depression of the left, and compression of the right; both frontal horns filled: oblique displacement of the septum lucidum, which is in line with displaced third ventricle, suggesting that the lesion is frontal rather than temporal—in which case the displaced septum lucidum remains vertical.



FIG. 225 (*b*).—Lateral, projection recumbent: flattening of roof of left ventricle.

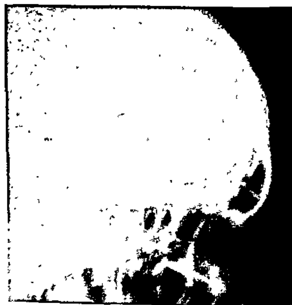


FIG. 226.—Lateral, projection supine; well-defined rounded filling defect in roof of ventricle almost completely obturating body, but frontal horn well filled. (Case of large deep glioma in right post-frontal and pre-parietal area; verified.)

apparatus is necessary. Information sufficient for ordinary purposes can be obtained from one or two films with a simple efficient plant.



FIG. 227 (*a*).

(*a*) *Technique*

The opaque medium may be introduced into the common or into the *internal carotid artery on one or both sides according* to the needs of the case. Common carotid injection will demonstrate both the internal and the external carotid circulation, and this may be an advantage when the tumour is a meningioma, in order to determine surgical procedures. Smaller quantities of medium can be used when the internal carotid is selected.

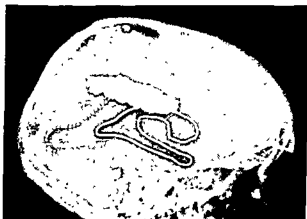


FIG. 227 (*b*).

FIG. 227 (*a*), (*b*), (*c*).—Displacement of ventricular system to left—affecting all portions of right lateral ventricle, but maximum about middle one-third of body, which is compressed and herniated under the falx cerebri—and dilatation of the left lateral ventricle. Typical findings in a case of chronic right subdural haematoma. (In the lateral projection the large faint shadow is of the dilated left vestibule and occipital horn; the anterior part of this ventricle is not filled, the air having escaped into the right ventricle, which in this projection lies above the left.)



FIG. 227 (*c*).

Exposure of arteries

The patient receives a sedative and the operation is performed under local anaesthesia. The common carotid artery is exposed through a transverse incision just above the clavicle by separating the sternal and clavicular

heads of the sternomastoid muscle. The internal carotid artery is exposed through an oblique incision higher in the neck, at or just above the bifurcation of the common carotid. A loop of tape is placed around the vessel, haemostasis perfected, and the wound suitably covered to avoid infection while the patient is transported to the x-ray room. During the exposure of the film the patient lies supine with the homolateral shoulder raised on a sand-bag so that the head can be turned sideways, enabling a lateral projection to be made with the side to be injected uppermost. When all adjustments have been made the wound is uncovered, the artery is gently brought into view on the tape, it is punctured and as soon as blood enters the syringe the Thorotrast is rapidly injected. The exposure should be made after approximately two-thirds of the total quantity of fluid has left the syringe. At least 10 cubic centimetres are needed for injection into the common carotid but 7 and even 5 cubic centimetres will suffice for internal carotid injection if the timing of the exposure is correct. Various shapes of needle have been specially designed; in order to ensure rapid injection the needle should be made of thin-walled tubing giving as large a bore as possible compared with the external diameter, and yet not making an excessive puncture wound in the artery. Bleeding from the artery is controlled by gentle pressure and stops within a minute or so. Direct percutaneous puncture of the artery is employed in some clinics, but considerable experience is needed to acquire the requisite skill. A simple tunnel and changing device can be constructed (Timins, 1943a) enab...g a second film to be exposed two seconds after the first; this will demonstrate the filling of veins. In some cases it may be considered desirable to make the projection antero-posterior rather than lateral, and by using two tubes and careful screening, it is possible to take an antero-posterior and a lateral projection simultaneously (Timins, 1943b).

Thorotrast Injection

Needle

(*b*) *Indications*

(i) To localize an expanding lesion.

(ii) To demonstrate the degree of its vascularity and the origin of the chief vessels; this may give information as to its pathology, for example meningioma, glioblastoma and astrocytoma.

(iii) To confirm the presence of and to localize aneurysms.

(iv) To confirm the presence of and to localize angiomatous malformations.

(*c*) *Dangers*

(i) Thorotrast is slightly radio-active; it is not excreted by the body, but it is held in the reticulo-endothelial system. However, the small quantities (10–20 cubic centimetres) used in the procedure probably have no significant deleterious effect upon the body. Experimental work has shown that in contact with mesoblastic tissue it can give rise to sarcoma; therefore great care must be taken that none is spilt in the wound.

Radio-activity

(ii) Thorotrast is capable of blocking the smaller cerebral vessels around a tumour or an abscess (Northfield and Russell, 1937).

Pyelosil, 35 per cent, has been used instead of Thorotrast and although it

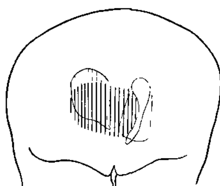
Pyelosil



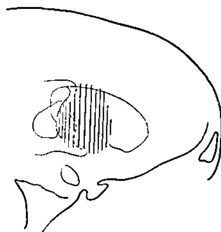
FIG. 228 (*a*).—A-P. projection, supine: right frontal horn not filled, but the body of this ventricle is dilated and its inner margin is ill-defined and imperceptibly blends with widened septum lucidum whose left margin is deflected to the left. The body and anterior horn of left ventricle are well filled, dilated, displaced slightly to the left, and there is a well-defined shadow impinging on medial boundary. Third ventricle not filled.



FIG. 228 (*b*).—Lateral projection, supine: only one anterior horn (the left) is filled and the air shadow is less dense in its posterior part corresponding to filling defect already seen in its inner wall; the smooth posterior margin of this filling defect is well shown. The faint and irregular outline of the posterior margin of the tumour which has obliterated the right frontal horn can be discerned, and was confirmed in other projections; third ventricle not filled.



(*a*)



(*b*)

FIG. 229 (*a*), (*b*).—Tracings of these projections (FIG. 228 (a) and (b)), with shading to indicate position of tumour; its superior, inferior and right lateral limits are conjectural. (Case of intraventricular right frontal tumour, invading septum lucidum and probably basal ganglia, obstructing foramina of Monro; exposed at operation but histological verification lacking.)



FIG. 230.—Encephalogram in a case of epilepsy following extensive compound depressed fracture in left frontal region. There is dilatation of both lateral ventricles, with additional enlargement of the left frontal horn towards site of injury; the septum lucidum is deflected slightly to the left side



(a)



(b)

FIG. 231 (a), (b).—Full encephalogram, performed approximately two years after a severe closed head injury. Dilatation of ventricles and of subarachnoid spaces over cortex, due to the shrinkage of brain substance.

gives a less dense shadow than the latter, it appears to be free from deleterious effects. The dangers of Thorotrast have given angiography a bad reputation, but it is probable that as Pyelosil replaces Thorotrast this valuable method of investigation will be used more frequently.



FIG. 232.—Normal arteriogram: a, anterior cerebral artery; b, middle cerebral group of arteries; c, cavernous portion of internal carotid artery.

(iii) The carotid artery may be lacerated by faulty technique or in cases in which its wall is diseased.

(5) *Minor exploratory procedures*

(*a*) *Ventricular estimation*

In an emergency, or when the facilities for ventriculography are not available, there is an alternative method of judging the normality or otherwise of the lateral ventricles. *Burr holes* Burr holes, equidistant from the middle line, are made in the frontal or parieto-occipital regions, and each lateral ventricle is tapped. The symmetry or otherwise of the needles and the depth of each ventricle will indicate whether the system is displaced, and the amount of ventricular enlargement. If one ventricle is compressed, such as by a tumour, much less fluid will flow from that needle than from the other, and indeed the ventricle may not be found. This procedure is very valuable in such cases as suspected frontal abscess or cerebral compression by a subdural haematoma, when the diagnosis and the lateralization of the lesion may be uncertain.



FIG. 233.—Normal phlebogram; the ascending frontal and parietal veins are filled; the large sinuous vessel entering the lateral sinus is the anastomotic vein of Labbé. The superior sagittal and lateral sinuses are indistinctly seen.

In some cases it may be desirable to make frontal and parietal burr holes so as to make a more thorough ventricular estimation and subdural exploration.

(b) Cystography

Nature of fluid

Exploratory needling of a suspected tumour may reveal a cyst. If the fluid is yellow and clots spontaneously on standing, the cyst is probably gliomatous; if it is opalescent and contains cholesterol crystals the fluid comes from an epidermoid cyst; the fluid from a porencephalic cyst is clear and colourless, and on analysis is identical with cerebrospinal fluid.



Fig. 234.—Arteriogram; aneurysm arising at the point of origin of the posterior communicating artery from the internal carotid artery.

Cyst injection

When a cyst is encountered useful information can be obtained by injecting into it an opaque medium (air, Thorotrast or Pyelosil) and subsequently taking skiagrams (Fig. 236). These will indicate precisely the location, shape and size of the cyst, and it is often possible to decide whether or not the tumour is malignant; in the latter case the shadow of the cyst wall is seen to be irregular and shaggy, whereas in the more slowly growing glioma it is usually smooth and rounded.

A similar procedure is employed in cases of abscess (Fig. 237 (a), (b)). When clear colourless fluid is obtained suggesting that a cyst is porencephalic, only air should be injected in case the cyst communicates with the ventricle.



Fig. 235.—Arteriogram; displacement forwards of the terminal portion of the internal carotid artery, and forwards and upwards of the anterior part of middle cerebral group, where the branches are approximated.

(c) Biopsy

When a space-occupying lesion is localized, which on clinical grounds is thought to be a glioblastoma, biopsy is advisable in order to confirm this; at the same time this will exclude conditions amenable to surgery such as chronic subdural haematoma, abscess and meningioma. A burr hole is made in the skull over the site of the suspected tumour, the dura mater opened, and a large-bore brain needle inserted into the brain. The tumour may be detected by a sense

Resistance to needle

of increased resistance to the needle or, if it is necrotic, by diminished resistance. A small quantity of the tissue is sucked into the needle by aspirating with a syringe, the needle withdrawn and the contents expelled with the stilette. If the tissue

Appearance of tissue

appears to be normal white matter, other attempts are made in different directions. Tumour tissue may be translucent, grey or yellow in appearance, or it may consist of necrotic debris; it is smeared on a glass slide, fixed in alcohol and examined histologically (Russell, 1939). Biopsy

Risk of bleeding

by needling may prove rapidly fatal in cases of glioblastoma as the result of bleeding into the tumour.

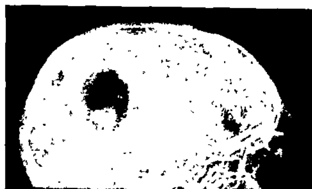


Fig. 236.—Cystic cavity in left occipital spongioblastoma multiforme; air and Thorotrast have been injected; the latter coats the irregular and shaggy tumour tissue.



Fig. 237 (*a*).—Right temporal abscess containing Thorotrast; an osteoplastic decompression has been performed.



237 (*b*).—Twenty-five days later, showing diminu- in size of abscess and formation of smooth wall.

(6) Electroencephalography

By means of thermionic amplification it is possible to study the electrical activity of the cortex of the brain; leads are taken

Electrodes

from electrodes suitably placed on the unshaven scalp, the records being made on a moving strip of paper by an ink-writing mechanism. Two electrodes are usually linked to one ink writer thus comparing the changes of potential between these points, and up to six records may be made simultaneously. In a normal resting subject

with the eyes closed, a characteristic rhythm synchronous in each hemisphere is found in the parieto-occipital region (Fig. 238 (a)); it consists of a sinusoidal curve having a frequency of about 10 cycles per second, and an amplitude of up to 100 microvolts; if the eyes are opened, or the subject meditates, the rhythmic discharge is inhibited. This activity was first described by Berger, and is now termed the alpha rhythm. Other rhythms of smaller voltage also occur in the cortex in health. Abnormal potential changes arise in a variety of conditions—cerebral anoxia, coma epilepsy and psychopathies; and in brain trauma, brain tumour and in other expanding intracranial lesions. In the latter group, the abnormality common to all is the development of a rhythm slower than the alpha, with usually a wider amplitude (Fig. 238 (b)). This "delta" discharge has a frequency of from 1 to 4 cycles per second, and it is indicative of damaged nerve cells. The more rapid in development and the more widespread the lesion, the greater will be the amplitude, that is the

Rhythm

Abnormal changes

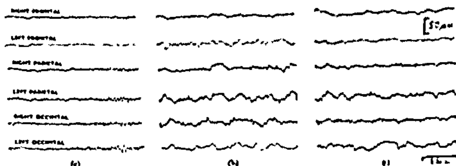


Fig. 238.—(a) Normal E.E.G. This shows a dominant frequency of 11 a second arising in the parieto-occipital region without any abnormal slow waves.
(b) E.E.G. in a case of left posterior parietal tumour, slow waves with frequencies ranging from 1 to 4 a second seen on both sides, but have highest voltage and maximal persistence in the left parietal lead.
(c) E.E.G. in a case of gunshot wound of the left parietal lobe 10 months previously. Records show a low-voltage dominant frequency of 11 a second on the right, with medium-voltage 2 a second waves in the left parietal and occipital areas.

greater the number of disturbed nerve cells discharging synchronously. The more severe the impairment of function the slower is the frequency of the potential changes, until eventually electrical activity ceases; leads from the scalp immediately over a large superficial tumour may record a straight line. The detection of such a silent area for purposes of localization is uncommon, but the localization of a delta discharge is of considerable value, for if the area from which such a record is obtained is carefully investigated a focus of "phase reversal" may be detected. Two pairs of leads are taken from three electrodes, the central electrode being common; the potential changes either side of this common electrode can thus be compared, and a point sought where the delta waves from one pair of leads are the mirror image of the other pair. Other frequencies, 4–7 cycles per second, may be encountered above a deeply situated tumour, and also in the temporo-parietal region. Although these positive localized abnormalities are valuable in the detection and the localization of a lesion, records apparently of a less definite kind may be indirectly helpful. Thus the finding of an abnormal electroencephalogram

"Phase reversal"

Cerebral tumours

from both frontal lobes in a case in which clinically the diagnosis is quite certainly a frontal lobe neoplasm would be strongly in favour of the tumour having spread bilaterally or being in the corpus callosum. Again a normal electroencephalogram in a case of suspected tumour may mean that the tumour is deep in the parasagittal region, where normal records may be found, or that it is a meningioma, for a slowly growing tumour of a non-infiltrating character frequently causes no disturbance of the electroencephalogram. Abnormal discharge of epileptic type when consistently localized to a particular area suggests an epileptogenic focus, though the electroencephalogram will not indicate the pathological nature of the lesion. During the early stages of recovery from a closed head injury, in which the patient has had concussion, slow waves may be recorded from all over the scalp. In penetrating injuries without generalized disturbance of brain function a similar electroencephalogram may be obtained from the immediate zone of injury (Fig. 238 (c)). Subsequently the slow waves subside, being gradually replaced by the normal frequencies. In the transitional period a temporary dysrhythmia may be seen similar to the electroencephalogram of epilepsy, and overt fits may occur. Both clinical and electroencephalographic experience show that prognosis in these cases of early post-traumatic epilepsy is good, in contrast to those cases in which after a return to normal, an abnormal record appears, and fits may or may not occur in conjunction with this change in the electroencephalogram. During the period of recovery from brain injury the subsidence of the delta discharge from a particular area may lag, suggesting that a maximal degree of trauma has been sustained at this point. In some cases the electroencephalogram may be normal except for a silent area, and this may indicate a subdural haematoma, an area of long-standing damage to the brain, or gross absence of brain tissue.

Head injury

The radiographs are reproduced by kind permission of Dr. M. H. Jupe, Director of the Radio-diagnostic Department, London Hospital. For the electroencephalographic records, we are indebted to Dr. Denis Williams, National Hospital for Nervous Diseases.

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BRAIN—TUMOURS AND TECHNIQUE

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PART I
SYMPTOMS, PATHOLOGY AND DIAGNOSIS

PART II
TREATMENT

PART I
SYMPTOMS, PATHOLOGY AND DIAGNOSIS

1. THE GENERAL EFFECTS OF INCREASED INTRACRANIAL PRESSURE

76.] The two chief effects of intracranial tumours are to raise intracranial pressure and to damage, by compression or destruction, nearby parts of the brain or cranial nerves. The volume of the cranial cavity is just sufficient to accommodate the brain, with its membranes, blood-vessels and cerebrospinal fluid. Any space-occupying lesion, whether tumour, abscess or haematoma, may develop unnoticed for a time by displacing cerebrospinal fluid and perhaps also circulating blood, but eventually the limit of this compensation is reached and the intracranial pressure begins to rise.

Headache

At this point the patient begins to complain of slight headache which becomes progressively more severe and frequent, and is often of a throbbing or bursting character. Vomiting and giddiness may occur with the headache or at times apart from it. In the early stages the mentality is clear, but as the pressure mounts the patient may become apathetic about himself and his surroundings, incontinent of urine and then of faeces; later there are phases of stupor which merge gradually into final coma.

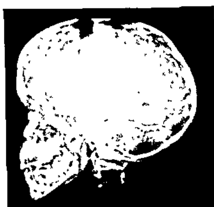


FIG. 239.—Separated sutures (particularly the coronal suture) and increased convolutional markings in a child aged 6 years with glioma of cerebellar vermis.

Objectively, the increase in pressure can be demonstrated by lumbar or ventricular manometry (normal is 150–180 millimetres of cerebrospinal fluid with the patient relaxed in the horizontal position). It can be inferred by detecting papilloedema, although the pressure may be raised for some weeks before changes in the fundi are manifest.

Visual symptoms

The patient may describe attacks of mistiness of vision: such transient amblyopic attacks usually signify marked papilloedema which, if untreated, goes on to secondary optic atrophy and blindness. Once a patient becomes blind from increased intracranial pressure, headache often lessens and may cease altogether. Other objective effects are squint and diplopia (usually due to stretching of the sixth cranial nerve, with paralysis of one or both external

rectus muscles); slowing of the pulse rate; elevation of the blood-pressure; and, in later stages, slowing of the respiratory rate. In females menstruation may become irregular or may cease; males sometimes become impotent. In some cases the sense of smell is impaired or lost, due to pressure of the frontal lobe upon the olfactory bulbs and tracts.

X-ray appearances

Additional objective evidence of increased intracranial pressure may be revealed by x-ray examination of the skull. In childhood, when the sutures have not united, the skull expands, (Fig. 239) and for a time this compensation may be adequate to prevent symptoms of increased pressure. Separation of the sutures is responsible for the "cracked-pot" note when the skull is percussed. Skiagrams show the separation, and the inner table of the vault may be thinned in a beaten-silver pattern. In adults the skull does not expand, but the vault may show the beaten-silver appearance, and rarefaction of the bone is obvious in thinning or destruction of the posterior clinoid processes.

"Cracked-pot" note on percussion

2. LOCAL EFFECTS

Localization of the lesion depends upon the focal neurological abnormalities produced by local pressure upon or destruction of neural elements by the tumour. Either general or local effects may predominate in any given case: thus, a patient with a large tumour in one cerebral hemisphere may have a profound sensori-motor hemiplegia without any headache, papilloedema or other sign of increased pressure. Another patient with a similarly situated tumour may have prostrating headache and gross papilloedema, with little motor or sensory disturbance. A full neurological examination, however, is important in every case. Investigation starts with the history carefully taken both from the patient and from his relatives and associates. The time-relations of his various symptoms are important, because in intracranial tumours the illness is almost always progressive, and from the earliest symptom it is possible to estimate the age and thence the type of the tumour.

Neurological examination

Epilepsy

Some type of epileptic attack occurs in a large proportion of cerebral tumours. These attacks may be of momentary unconsciousness, but more commonly are generalized convulsive seizures, like those of idiopathic epilepsy, without any obvious focal manifestations. However, tumours in certain situations may produce attacks which have a recognizably focal pattern; thus, a tumour in or near the motor cortex produces localized clonic contractions of one limb, or of the face and limbs on one side of the body. If the sensory cortex is involved, paraesthesia may replace or precede the muscular contractions of the focal motor attack. Frontal lesions anterior to the precentral gyrus may cause attacks in which the head and eyes are turned forcibly to the opposite side. In the temporal lobe, lesions near the medial surface are often associated with uncinate attacks, characterized by olfactory or gustatory hallucinations, which may occur without loss of consciousness or may constitute the aura of a generalized convulsion. Temporal lesions may also produce highly organized visual or auditory hallucinations—complex scenes or sounds which the patient may be unable to describe, or unwilling to admit to for fear he may be regarded as being mentally deranged. In occipital lesions there may also be visual hallucinations, but these are usually cruder, consisting of flashes of light or

Hallucinations

coloured spots which may be referred to the opposite homonymous field of vision. With lesions in the posterior fossa there may be attacks of hyperextension of the head, with altered breathing, extensor rigidity of the limbs and usually momentary loss of consciousness.

Tumours in the speech-dominant hemisphere often interfere with speech, *Aphasia* especially those near the Sylvian fissure. Aphasia may occur in attacks, or it may be constant and progressive. Expression and the understanding of the spoken and written word and symbol are usually affected, but one aspect of speech may be predominantly involved. The disturbance may be gross enough to hinder contact with the patient, or so slight that it is only detectable in formal tests of the patient's ability to name promptly a large series of common objects.

A tumour in one frontal lobe may present few, or no focal signs, but if both *Frontal lobe* frontal lobes are involved there is commonly intellectual impairment progressing to gross dementia, and the same is true of tumours of the corpus callosum. In the speech-dominant hemisphere it may be important to differentiate apparent dementia from aphasia, as the patient's speech and behaviour may be largely determined by his language difficulty. Farther back in the frontal lobe some degree of contralateral paralysis results from involvement of the motor pathways. Tumours in the lower part of the frontal lobe cause paralysis of the opposite side of the face, arm and leg, in that order, whereas in those beginning near the supero-medial margin of the hemisphere the order is reversed.

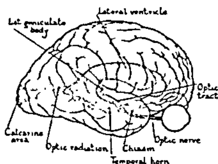


FIG. 240.—The central pathways of vision. (*After Adolf Meyer and Max Brödl.*)

Tumours of the parietal lobe interrupt the sensory and visual pathways. *Parietal lobe* The sensory impairment affects the opposite side of the body, or a part of it, and chiefly the discriminative modalities: these are postural sensibility, stereognostic sense, and the ability to discriminate between one and two points of a compass, or between different textures. Cutaneous sensation may also be affected, but not grossly as with spinal or peripheral nerve lesions; light touch, painful stimuli and thermal stimuli are felt, but not accurately. Rarely, painful stimuli produce a "thalamic" response: the threshold to the *"Thalamic" response* stimulus is raised, but once it is attained the stimulus evokes an excessive response, light touch becoming unpleasant, painful stimuli causing more pain than on the sound side and in a more diffuse area. In parietal tumours the upper part of the optic radiation may be compressed (Fig. 240), the characteristic defect in the visual fields being an homonymous lower quadrant hemianopia, but if the lesion is situated deeply in the hemisphere the homonymous hemianopia may be complete.

A visual field defect may be the only sign in tumours of the temporal lobe. *Temporal lobe* Characteristically, it is an upper quadrant hemianopia due to involvement of the lower part of the optic radiation. The defect may be so slight that careful perimetry is required to detect it, but in extensive or deeply placed tumours

there may be a complete hemianopia easily demonstrable in confrontation tests. Tumours with complete homonymous hemianopia as their first local sign are usually situated on the inferior aspect of the temporal lobe, a situation which is rather inaccessible. Aphasia is common in lesions of the temporal lobe of the speech-dominant hemisphere, but it has not the precise localizing value of the characteristic visual field defect. As the tumour enlarges some degree of paralysis and sensory disturbance is common, the opposite face, arm and leg being affected, in that order.

Occipital lobe

Occipital tumours often produce no focal signs except homonymous hemianopia, which usually affects the lower quadrants first, but as the tumour extends forward there may be some sensory disturbance and later loss of power in the opposite side of the body.

Intraventricular tumours

Intraventricular tumours (including those growing in the basal ganglia) produce no constant clinical picture; from their situation they may obstruct the circulation of the cerebrospinal fluid and cause intermittent hydrocephalus with a great increase in intracranial pressure, and yet no obvious focal abnormalities; or, if they are in the inferior or posterior horn of the lateral ventricle they may grow to a large size without producing any signs of raised intracranial pressure. Attacks of drowsiness may be frequent and the protein content of the cerebrospinal fluid may be high. In most cases the localization can only be established by ventriculography.

Pineal region

Tumours in the region of the pineal gland and quadrigeminal plate produce oculomotor signs—paralysis of conjugate upward movement of the eyes, ptosis, and weakness or paralysis of the pupillary reaction to light. Hydrocephalus and general pressure signs are early, because of obstruction to the aqueduct of Sylvius, the narrowest part of the ventricular system. Some pineal tumours of infants produce sexual precocity.

Brain stem

Tumours of the brain stem (midbrain, pons and medulla oblongata) generally produce striking neurological abnormalities for some time before there are any signs or symptoms of increased intracranial pressure. Multiple cranial nerve palsies are common, and so is involvement of the long sensory and motor tracts traversing the brain stem, and of the cerebellar connexions. Usually the signs are bilateral, although the effects may be remarkably confined to one side. The presence of "crossed" paralysis is strongly suggestive of an intramedullary lesion, for example, paralysis of one or more cranial nerves on one side, with paralysis and sensory disturbance in the opposite limbs.

"Crossed" paralysis

Cerebellum

Cerebellar tumours usually produce symptoms and signs of increased intracranial pressure early in their development because of the small capacity of the posterior cranial fossa and the tight fit at its two major apertures, the foramen magnum below and the incisura tentorii above. An expanding lesion tends to cause impaction at one of these apertures, or blockage of the lower end of the aqueduct of Sylvius, with a rapid increase in intracranial pressure. Tumours of the vermis and of the lateral lobe of the cerebellum may produce few or no signs of cerebellar dysfunction, but in tumours which extend deeply enough to involve the cerebellar peduncles local signs are fairly constant. These signs are defective conjugate movement of the eyeballs towards the side of the lesion with nystagmus, which is slow and coarse on looking towards the side of the lesion and rapid and finer on looking towards the

opposite side, hypotonia, ataxy, dysdiadokokinesis, and slight weakness of the limbs on the side of the lesion and unsteadiness of gait and of the trunk, with veering to the side of the lesion. Pressure upon the medulla and lower cranial nerves causes dysarthria and dysphagia, and vomiting is common, especially with tumours involving the fourth ventricle.

Dysarthria and dysphagia

Cerebello-pontine angle

Cerebello-pontine angle tumours affect first the cranial nerves in the angle and later on the cerebellum and its connexions. The common acoustic neurinoma of the eighth nerve causes unilateral deafness and abolition of the normal vestibular responses to the cold caloric test; facial palsy, trigeminal sensory impairment, and often strabismus due to paralysis of the sixth nerve. Apart from eighth-nerve signs these cranial nerve palsies may be slight. Nystagmus is constant, even in the early stages. As the tumour grows, slight to moderate degrees of unilateral cerebellar dysfunction become manifest. There are usually signs of raised intracranial pressure and in some cases these may predominate. Generally the protein content of the cerebrospinal fluid is increased. Skiagrams may show erosion or enlargement of the internal acoustic meatus but this is not constant.

From the foregoing considerations it is evident that some intracranial tumours can be easily recognized and located by thorough clinical investigations, while in other cases accurate localization by clinical methods is difficult if not impossible.

Fortunately in these cases localization and sometimes pathological diagnosis can be made by means of accessory methods—skiagrams of the skull, ventriculography and cerebral angiography.

3. PATHOLOGY

Benign tumours

Malignant tumours

The prognosis of the lesion largely depends upon its pathology. Some tumours are histologically benign, and can be completely and permanently removed with full recovery of the patient. Others are histologically malignant, and because of their nature and situation cannot be completely removed. In these subtotal operations the tumour invariably recurs locally, and occasionally in other parts of the cerebrospinal pathways. Metastases of primary intradural tumours outside the central nervous system are virtually unknown.

Often the type of tumour cannot be known until operation, when it may be easily recognizable by the naked eye or must be determined by a rapid histological examination, as with the wet-film technique (Russell, Krayenbuhl and Cairns, 1937).

Meningioma

The meningioma is usually easy to recognize because it grows from the meninges, and although it may become embedded in the brain some part of it is usually visible on the surface (Fig. 241). It is a firm, often lobulated, encapsulated mass of reddish or greyish-red colour and of variable firmness, which can be stripped from the surrounding brain once the dural and arachnoid membranes are divided round its margins. Sometimes it is calcified. It has certain special sites of origin—alongside the sagittal sinus; in the anterior fossa along the olfactory groove, or at the tuberculum sellae; along the sphenoidal ridge; and in the cerebello-pontine angle. Occasionally it arises in the choroid plexus of the lateral ventricle.

These tumours are usually very vascular, drawing their blood supply from

the cerebral and the meningeal vessels, and abnormal meningeal vascular patterns may be visible in skiagrams of the skull. At the site of attachment the tumour often produces a localized hyperostosis on the inner table of the skull (Fig. 241) which maybe visible in skiagrams; occasionally the hyperostosis contains tumour cells. Some meningiomas spread freely from the dura to the

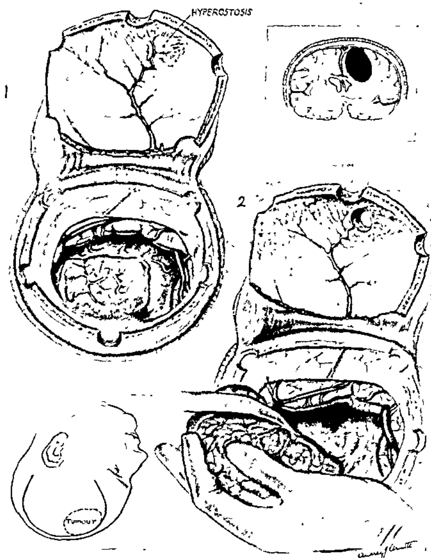


Fig. 241.—Left frontal parasagittal meningioma, showing hyperostosis and increased vascular markings from enlargement of meningeal vessels. (2) Shows removal of tumour; the hyperostosis has been destroyed by burring.

overlying skull, producing a bony lump visible on the outer table of the skull (Fig. 242). All these endostoses require removal to prevent recurrence of tumour, but in the base of the skull they may be too extensive for complete removal. Furthermore, a meningioma in the floor of the skull may invade the cavernous sinus or grow round the vessels of the circle of Willis in such a manner that complete removal is impossible. With these exceptions, they

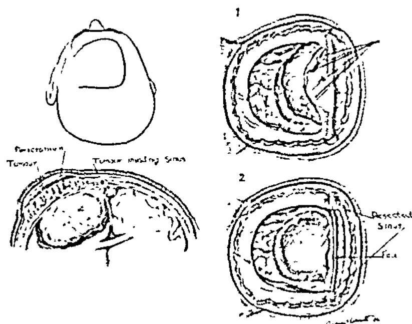


Fig. 242.—Left frontal meningioma with invasion of overlying skull and sagittal sinus. (1) Shows the bony tumour removed; (2) the intracranial part of the tumour removed, together with 8 centimetres of the sagittal sinus which was invaded by the tumour. The patient was well and at work 4 years later.

are benign tumours and among the most favourable for surgical treatment. Of 686 cases of intracranial tumour verified at operation in the Nuffield Department of Surgery, 13·8 per cent were meningiomas.

Gliomas

Almost half (47·8 per cent) of all intracranial tumours are gliomas. These tumours grow within the substance of the brain and may be malignant or benign. The malignant gliomas which are the more common are composed of primitive types of neuroglial cells showing varying degrees of differentiation. The more adult the type of cell the slower the growth and the less the invasive powers of the tumour. But some tumours are relatively well differentiated in one part and poorly differentiated in another. The benign gliomas are composed of adult types of cell, are circumscribed and do not recur after surgical removal.



Fig. 243.—Spongioblastoma multiforme of frontal and parietal lobes, invading corpus callosum.

Spongioblastoma multiforme

Of the malignant gliomas spongioblastoma multiforme (Fig. 243) is by far the most common. It is a soft vascular tumour often containing cysts and areas of necrosis. Although the main mass of the tumour may appear to be fairly well circumscribed there may be considerable extension into the surrounding

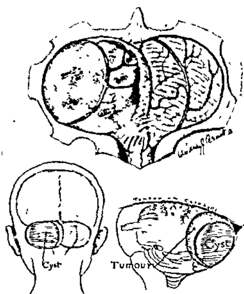


FIG. 244 (a).—Cystic and solid cerebellar astrocytoma. The patient, a male aged 13 years, was well and at work 10 years after its removal.

white matter, and the same is true of other malignant gliomas, such as cerebral astrocytoma and oligodendroglioma. Some of these gliomas may be partly or wholly calcified. The life history of spongioblastoma multiforme rarely exceeds 1 year, that of the other malignant gliomas is longer; but there are exceptions. Some of these gliomas respond favourably to radiation treatment.

Cerebellar medulloblastoma

Cerebellar medulloblastoma is a malignant glioma of childhood, composed of very primitive cells which may differentiate either into neurones or into neuroglia. This tumour is prone to spread in the subarachnoid space of the basal cisterns and spinal canal. It is for a time very sensitive to x-ray irradiation.

The benign gliomas are mostly astrocytomas (Fig. 244 (a)) and ependymomas (Fig. 244 (b)) of the cerebellum, but occasionally in the cerebral hemispheres also these tumours are not invasive and their removal is followed by freedom from recurrence for many years. The cerebellar astrocytoma is a firm homogeneous circumscribed mass, and it not infrequently has one or more large cysts into which the solid tumour projects as a mural nodule. The cerebellar ependymoma is also homogeneous and firm, it is often attached to the lower end of the floor of the fourth ventricle and expands upwards into the vermis and fourth ventricle, and sometimes also down into the cisterna magna as a tongue of tumour which passes through the foramen magnum.

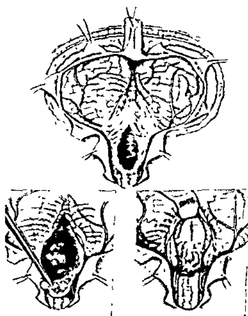


FIG. 244 (b).—Cerebellar ependymoma, attached to the lower end of the floor of the fourth ventrical which was removed subtotally from a female aged 47 years. The patient was subsequently free from symptoms, but died suddenly 3 years later.

Haemangioblastoma

Haemangioblastoma (3·2 per cent) is another benign tumour of the cerebellum (Fig. 245). It also may produce a large cyst into which the tumour projects as a small mural nodule; or, as with the astrocytoma, there may be a solid, fleshy

mass of great vascularity without any cyst formation. This tumour may be associated with angiomatous malformations in other parts of the body, notably in the retina (v. Hippel's disease) and the condition may be hereditary. In a patient with symptoms of a cerebellar tumour a history of brain tumour or retinal tumour in some other member of the same or a previous generation of the family favours the strong presumption that the patient is suffering from a haemangioblastoma.

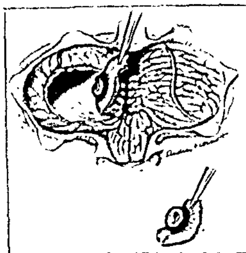


Fig. 245.—Cystic haemangioblastoma of cerebellum with small mural nodule of solid tumour.

Acoustic neurinoma

In the cerebello-pontine angle the commonest tumour is the acoustic neurinoma (11·3 per cent) which may occur as a solitary tumour or may be a manifestation of generalized neurofibromatosis with a familial tendency. It is a smooth, ovoid tumour growing from the eighth nerve and usually attached at the internal acoustic meatus. It has a definite capsule invested with arachnoid, and the interior is usually composed of soft, yellow, buttery material, interspersed with tougher areas. As it enlarges it becomes embedded in the adjacent cerebellum and pons. The external appearance may be very similar to a meningioma of the cerebello-pontine angle, although the latter is usually firmer, more vascular and does not grow from a cranial nerve but from a meningeal attachment.



Fig. 246.—Multiple carcinomas of cerebellum secondary to primary carcinoma of lung.

Metastatic tumours

Metastatic tumours may develop in any part of the brain and are often multiple (Fig. 246). As pointed out by Elkington they often occur at the junction of grey and white matter, and they form discrete nodules which are apparently sharply circumscribed. Necrosis is common and in some cases leads to the formation of cysts containing turbid brown fluid. The common sites for the primary tumour are lung, stomach, breast and prostate.

Some tumours occur only within the ventricular system. The commonest varieties are colloid cysts which develop in the third ventricle and produce hydrocephalus by obstructing the foramina of Monro in a ball-valve manner, and papilloma of the choroid plexus which may occur in any part of the ventricular system. Less commonly meningioma of the choroid plexus, teratoma and cholesteatoma are found within the ventricular system. All these tumours are benign.

4. DIFFERENTIAL DIAGNOSIS

Other expanding lesions

Many lesions produce the local and general effects of an intracranial neoplasm. Thus, a brain abscess or a chronic subdural haematoma, both expanding lesions, commonly cause increased pressure, and the pre-operative diagnosis from intracranial tumour depends upon knowledge of a likely source of infection in the one case (for example, mastoid or frontal sinus infection or intrathoracic sepsis), and knowledge of a head injury (usually a relatively mild one) in the other. Hydrocephalus due to stricture of the aqueduct of Sylvius, or to obstruction of the foramen of Magendie by a congenital septum or old meningitis, may produce symptoms like those of brain tumour.

Venous obstruction

Objective signs of increased pressure, such as papilloedema and high cerebrospinal-fluid pressure, may be produced by any lesion which obstructs the venous return from the cranium. The commonest, otitic hydrocephalus, is associated with mastoid disease although a similar state can occur with other infections, with pregnancy and the puerperium, and with injuries to the large venous sinuses. It is thought to be due to partial thrombosis of one or more of these sinuses, and is a benign process which tends to recover spontaneously as the clot in the sinus becomes canalized, though when there is high papilloedema sight may be permanently damaged if the rise of intracranial pressure is not relieved. Headache is generally not very severe, even though there may be four or five diopters of papilloedema, and the patient looks and feels much better than if he were suffering from a tumour. There are usually no focal signs, although if the thrombosis extends to the cerebral vessels there may be gross signs, such as hemiplegia, aphasia and hemianopia. Apart from its high pressure the cerebrospinal fluid is usually normal, the protein content being on the low side of normal.

Cerebro-vascular disease

Diseases of the cerebral blood-vessels causing haemorrhage and thrombosis are common problems in differential diagnosis. There may be gross focal abnormalities, such as hemiplegia and aphasia, but the onset is usually sudden, and if death does not ensue, some recovery of function may occur. On the other hand, with a neoplasm the onset is more gradual and the deterioration is usually progressive. With vascular lesions there is often evidence of widespread vascular disease in other parts of the body. However, haemorrhage from an intracranial aneurysm may occur in young subjects with otherwise normal vascular systems. Again, the onset is usually abrupt and lumbar puncture reveals subarachnoid blood. The commonest focal sign in such lesions is paralysis of one oculomotor nerve.

Arterial hypertension may cause headache very similar to that of increased intracranial pressure. Haemorrhages and exudates in the retina enhance the suspicion of an intracranial tumour. Pathological changes in the vessels usually with very little swelling of the disc for the amount of haemorrhage and exudate suggest arteriopathic retinitis. The blood-pressure is raised to critical levels and there are usually no focal abnormalities. It is obvious that a brain tumour may occur in a subject already suffering from hypertension, and diagnosis may only be settled by ventriculography.

Migraine

The headache and vomiting of severe migraine may be mistaken for symptoms of an intracranial tumour, but more commonly these symptoms of a tumour are mistaken for migraine. In migraine there is usually a history of

repeated attacks, with good health in the intervals, and there is no objective evidence of increased pressure, even at the height of the attack. There are no neurological abnormalities in the intervals between attacks, but there may be transient hemianopia, scotomas, paralyses or aphasia during the attack. There is often a family history of migraine or of an associated allergic disorder.

Epilepsy Epilepsy commencing in middle life is most commonly due to intracranial tumour, though it may be caused by vascular disease, poisoning by alcohol or other poisons, parasitic infestation, low-grade infections, presenile dementias, and other lesions. If there are no signs of raised intracranial pressure accurate diagnosis of the cause of the epilepsy may be very difficult, and encephalography, ventriculography or arteriography is often necessary.

Neuroses Many patients with constant or frequent headache and vague symptoms of giddiness, blurred vision, etc., may eventually be suspected of having a brain tumour. Absence of objective abnormalities, combined with many subjective complaints, especially in a person predisposed to neurosis, usually indicates only neurosis, but once suspicion of brain tumour has been raised it requires a full investigation, including x-ray examination, lumbar puncture and in some cases ventriculography, to exclude a space-occupying lesion, and such an investigation is often an essential part of treatment.

PART II
TREATMENT

1. VARIETIES OF OPERATION

Treatment varies according to the type of tumour. Complete removal is not always possible. Malignant tumours can rarely be sufficiently delimited for complete removal and a minority of the benign tumours are so situated that complete removal would damage important parts of the brain. In such cases incomplete operations, which would not be contemplated in tumour surgery in other parts of the body, may be inevitable. They are often remarkably effective in relieving symptoms—in malignant tumours for a few months only, in benign tumours sometimes for years. Operations for intracranial tumour fall into the following groups: (1) complete removal; (2) partial removal; (3) decompression (subtemporal, cerebellar); (4) internal decompression; (5) short-circuiting operations (such as ventriculo-cisternostomy); (6) diagnostic operations. Choice depends upon the pathological diagnosis established by clinical examination, special investigations and in some cases by direct inspection of the lesion.

(1) Complete removal of the tumour

With adequate attention to technical details, benign tumours can usually be completely removed. Excessive blood loss or difficulties of exposure may require that the operation shall be completed in stages. Practically all meningiomas, haemangioblastomas, cerebellar astrocytomas, dermoids, cholesteatomas, colloid cysts of the third ventricle and other rarer benign tumours should be treated by complete removal. Some cranio-pharyngiomas and acoustic neurinomas should also be completely removed. The functional

results should be satisfactory if there is no damage to nearby important structures and no post-operative infection, and if the operation is undertaken before the patient's functions, and particularly his vision, have been irreparably damaged.

(2) Incomplete removal of the tumour

In certain benign tumours incomplete removal will give a better functional result. Thus, in pituitary adenoma removal of the tumour should be radical enough to relieve pressure on the optic chiasm, but complete extirpation may produce pituitary cachexia. In cranio-pharyngiomas parts of the tumour may have to be left because of their firm adhesion to such essential structures as the floor of the third ventricle or the anterior cerebral arteries. In acoustic neurinoma complete removal usually means permanent facial palsy on the corresponding side; if the facial nerve is to be preserved intact, part of the capsule of the neurinoma must usually be left behind. On the other hand, in such cases, partial removal of the tumour may mean recurrence of symptoms later. The right course in each case can only be decided from an intimate knowledge of the patient's functional and personal problems, based upon thorough clinical studies. To be effective these incomplete removals should re-establish the circulation of the cerebrospinal fluid in the region of the tumour. At the end of subtotal extirpation of a tumour the brain should be slack and cerebrospinal fluid should be welling up from the region of the tumour bed.

Each case an individual problem

In malignant gliomas, apparently complete removal rarely proves to be so. As Scherer has shown, there may be extensions of tumour through the corpus callosum from one hemisphere to the other which are not visible to the naked eye. Even with very radical operations involving mutilation of healthy brain tissue, symptoms often recur as quickly as in cases in which removal of the tumour is overtly incomplete. In many of these cases operation has little to commend it, but all the visible tumour should be removed in order to obtain the maximal relief of raised intracranial pressure. For example, in medulloblastoma of the cerebellar vermis associated with high papilloedema, a reasonably good temporary functional result will follow x-ray treatment, provided preservation of sight is first ensured by operative reduction of raised intracranial pressure: in such a case cerebellar decompression alone may not relieve the obstruction of the fourth ventricle and aqueduct of Sylvius, and tumour tissue should be removed until the cerebrospinal fluid flows freely through the fourth ventricle. Malignant gliomas are sometimes very vascular and after biopsy or partial removal may bleed to such an extent, both externally and into themselves, that the only way to stop the oozing is to remove all visible tumour tissue.

In relatively benign but extensive gliomas, such as astrocytoma of the cerebral hemisphere, partial removal of that part of the tumour which occupies a silent area such as the frontal pole or the right temporal lobe is often indicated (Fig. 247).

(3) Decompression

Palliative operation

Decompression is a palliative operation to relieve raised intracranial pressure. Formerly it was applied indiscriminately to patients showing signs of

raised intracranial pressure from unlocalized tumour, but with the increased diagnostic precision which has resulted from greater knowledge of the various tumour syndromes, from radiography, ventriculography and angiography,

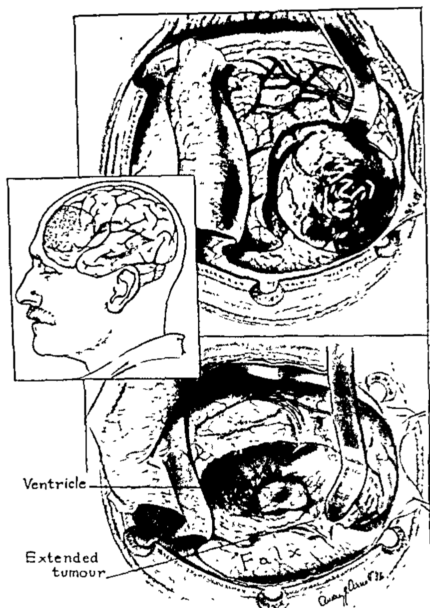


FIG. 247.—Incomplete removal of left frontal cystic and solid oligodendroglioma. At operation the tumour was found to extend beneath the falx into the corpus callosum and the right frontal lobe. The patient was subsequently treated by x-ray irradiation, and was well and working 4 years after operation.

the operation has been much less in evidence. Also the use of palliative decompression for malignant intracranial tumours has fallen into disrepute as it may prolong helpless invalidism. Nevertheless decompression may preserve vision in advancing papilloedema when the tumour cannot be removed—for

example, the inadequately exposed tumour (Fig. 248), or the tumour which should not be removed (for example, tuberculoma or pinealoma), or the tumour which cannot be found. The operation may give relief in tumour-like states with raised intracranial pressure—for instance in certain types of hydrocephalus of adults, some malformations of the skull, such as platybasia, and certain rare types of encephalitis. It is sometimes used as a preliminary to

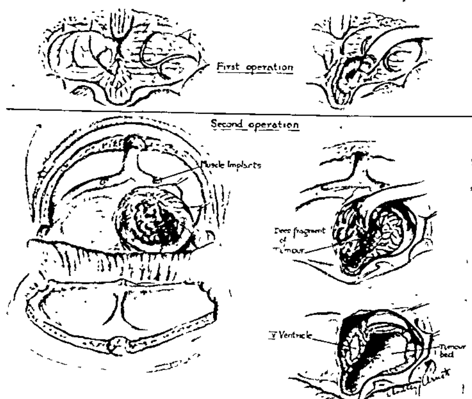


FIG. 248.—Cerebellar haemangioblastoma. At the first operation the cerebellum was exposed by the usual cross-bow approach. The tumour was found deep in the right lateral cerebellar lobe but the exposure was inadequate to enable it to be safely removed. As a result of the cerebellar decompression the patient's symptoms were relieved and his papilloedema subsided, with preservation of normal vision. One year later he became unsteady and papilloedema recurred. Through the same skin incision a bilateral occipital bone flap was reflected. This gave adequate exposure of a vascular tumour which was completely removed without difficulty. The patient was well and working 8 years later.

radiation treatment and in the course of treatment of certain acute and subacute brain abscesses.

Decompression over tumour

The maximal relief is only obtained if the decompression is over or very near the site of the tumour. Decompression at a distance from the tumour may not sufficiently relieve the rise of intracranial pressure to prevent blindness, particularly in cases already showing florid papilloedema; in some cases it may even result in dangerous shifts of the brain stem.

The unopened dura exposed by removal of bone can stretch slightly, as has

been shown in the treatment, by repeated aspiration and decompression, of acute and subacute brain abscess, but in the great majority of cases raised intracranial pressure can be satisfactorily relieved only by opening the dura. When the dura is opened the exposed brain is herniated through the dural opening. This gives rise to abnormal stresses in the herniated part and in the underlying brain, with the formation of cysts in the white matter, and a certain amount of destruction of brain tissue. Consequently decompression operations should be in silent areas, and the herniating brain should be prevented from projecting unduly by firm closure of the overlying muscle. The standard sites for decompression are the cerebellum (sub-occipital decompression) and the right temporal lobe (subtemporal decompression), parts of the brain which can be protected to some extent by the overlying muscle, and in which damage resulting from herniation does not usually produce symptoms. A decompression effect may also be obtained after osteoplastic exploration by opening the dura over the area of the tumour and replacing the bone flap loosely (osteoplastic decompression).

Standard sites for decompression

(*a*) *Sub-occipital*

This is the most effective of the standard decompressions. Three incisions are employed (Fig. 249 (a), (b) and (c)) of which the most usual is the simple bow incision. *The muscles of the back of the neck are divided transversely just* below the superior curved line of the occiput and are detached down as far as the posterior arch of the atlas, and out almost as far as the posterior margin of the mastoid processes. The exposed bone is then removed. When intracranial pressure is known to be severely raised it is wise to remove also the posterior arch of the atlas, though this may be left until the dura has been opened. Before opening the dura it is essential to reduce intracranial pressure by tapping the lateral ventricles. Once the dura is opened there should be no delay in releasing cerebrospinal fluid from the cisterna magna as until that is done the cerebellum is often bulging considerably even though the lateral ventricle has been tapped, and further progress of the operation is difficult. If the cerebellar tonsils are herniated severely it may even be necessary to remove the posterior arch of the axis before the cisterna magna can be opened; in such cases the exposure can be facilitated by adding a vertical midline incision, thus converting the bow incision into a cross-bow (Fig. 249 (c)).

Bow incision



FIG. 249.—Incisions employed for exposure of the cerebellum; (a) is the one most commonly employed (bow incision), and can be extended by adding a vertical limb (b) making a cross-bow incision (c) if it proves necessary to expose the lower part of the fourth ventricle or the upper part of the spinal cord more widely.

Closure of the cerebellar decompression should be meticulously carried out in layers. During the first 2–3 weeks after operation, it may be advisable to protect the suture lines from undue tension by frequent lumbar punctures. If the sutures give way, either from careless suturing, or excessive tension subsequently, the usual result is a subcutaneous bag of cerebrospinal fluid.

Closure of decompression in layers

(*b*) *Subtemporal*

The stages of this operation are shown in Fig. 250. Another method (Fig. 251) gives a wider decompression beneath the temporal muscle but has the disadvantage of interfering with subsequent osteoplastic exposure of the same hemisphere.

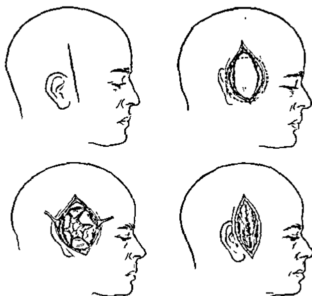


FIG 250.—Subtemporal decompression.

This operation used to be popular in the treatment of unlocalized tumours, but is rarely required now that diagnosis has become so precise. However, there is still occasional use for subtemporal decompression during the course of a lateral osteoplastic flap (Fig. 255 (c)).

(*c*) *Osteoplastic*

In the course of exploration for a tumour of the cerebral hemisphere by an osteoplastic flap a decompression effect may be required. (i) A tumour may be encountered which cannot or should not be removed. (ii) In a third-ventricle tumour requiring transventricular removal (Fig. 252) it may be desirable to allow the anterior horn of the lateral ventricle to dilate further for 2 or 3 months in order to obtain an easier approach to the tumour. In osteoplastic decompression the dura is left open, the exposed surface of brain is protected with fibrin film or sheet gutta-percha which is left *in situ*; the bone of the flap is replaced and loosely retained in place by pericranial stitches; the scalp is then firmly closed in two layers. This type of operation allows slight herniation of a fairly large area of brain without any of the severe brain destruction which may follow unprotected herniation.

Fibrin film or gutta-percha as protective layer

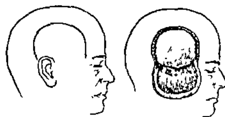


FIG. 251.—Subtemporal decompression (another method).

(4) Internal decompression

In malignant tumours of the cerebral hemispheres, as an external decompression may precipitate the onset of hemiplegia, McKenzie introduced the operation of internal decompression. After removal of the accessible part of the tumour, room is obtained for expansion of the remaining tumour by sacrifice of silent parts of the brain: for example, in frontal glioblastoma extending into the corpus callosum and not completely removable, the

anterior part of the frontal lobe can be amputated. The osteoplastic flap is wired firmly back in place. In suitable cases this type of operation may relieve symptoms fairly completely for a time, and when symptoms recur life is not uselessly prolonged by relief of pressure from herniation of brain.

(5) Short-circuiting operations

In certain slow-growing tumours of the third ventricle and midbrain region where removal may endanger life or function, hydrocephalus may be relieved by a short-circuiting operation. The most effective type is Torkildsen's

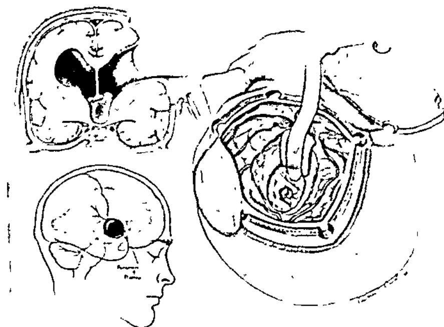


FIG. 252.—Transventricular removal of colloid cyst of third ventricle.

operation of ventriculo-cisternostomy, in which a rubber catheter or a plastic tube of acrylic resin or polythene is led from the posterior horn of the lateral ventricle into the cisterna magna and is left *in situ* (Fig. 253). If the tumour is radio-sensitive, as for example are most pineal tumours, the operation should be followed by x-ray irradiation of the region.

This operation is also effective in relieving hydrocephalus due to stricture of the aqueduct of Sylvius.

(6) Diagnostic operations

Operative explorations of the brain for tumour without reasonable certainty of identifying the tumour have now become rare, because diagnostic methods are so precise; in a few cases of the chiasmal syndrome and in early lesions in the region of the Rolandic fissure, however, the only way of excluding a removable tumour or some other operable lesion may be direct operative exploration of the region concerned.

Another diagnostic operation is that of needle biopsy which is employed to *Needle biopsy*

determine by histological examination the operability of a tumour, in cases in which from the rapid course or some other feature an inoperable malignant tumour is suspected. Through a burr hole a blunt brain needle is passed into the region of the tumour and then withdrawn with or without suction. Tiny fragments of tissue are usually found in the eye of the needle and from these a film of tissue is prepared on a slide, is fixed in formalin, and then stained with aniline dyes (the wet-film technique). From such films the presence and character of the tumour can be determined with reasonable accuracy, but if the method is to give satisfactory results it is essential that the needle should be passed into the right part of the brain. If needle biopsy is negative in a case of suspected tumour it is probably wise to check the clinical

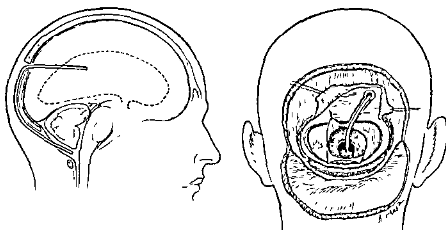


Fig. 253.—Ventriculo-cisternostomy (Torkildsen's operation).

localization of the suspect area by ventriculography or arteriography. Sometimes the diagnosis can be made without histological examination, for the needle encounters a cyst or an abscess, or the firm unyielding capsule of a meningioma. Like ventriculography, this method may be dangerous if not immediately followed by a major operation and removal of the tumour. In malignant tumours it may hasten the onset of severe symptoms, but for such cases there is usually no effective treatment.

2. EMERGENCY TREATMENT

Raised intracranial pressure

Urgent situations frequently arise from local or general increase in intracranial pressure. *The patient becomes stuporous or comatose and is likely to* stop breathing unless the excessive rise of intracranial pressure is promptly relieved. The excessive rise of intracranial pressure may be due to sudden complete blockage of the cerebrospinal pathways by a small tumour, such as a colloid cyst of the third ventricle, or to a tumour which has rapidly expanded as a result of haemorrhage or cyst formation. Sudden severe local rise of intracranial pressure may also be due to oedema of the white matter round the tumour; in such cases dangerous pressure may be exerted upon the brain stem, without great rise of the general intracranial pressure as measured in the lateral ventricles, by herniation of oedematous cerebral convolutions through the tentorial opening, by herniation of the cerebellar vermis upwards

through the tentorial opening, or by herniation of the cerebellar tonsils through the foramen magnum. Other herniations of cerebral tissue also occur which interfere with circulation of the cerebrospinal fluid. In some cases also, it is possible that intracranial pressure is suddenly and violently raised by obstruction to venous outflow of the brain from compression of the sagittal or lateral sinuses by nearby tumours. Slowing of respiration, as for example after an injection of morphine or from compression of the medulla oblongata, has a similar effect of raising cerebral venous pressure and thus further raising intracranial pressure.

Obstruction to venous outflow

Some warning of the onset of coma from raised intracranial pressure can usually, though not always, be obtained. For some hours the patient may have bouts of intense headache. Recurrent vomiting in a patient previously not subject to this symptom should always arouse suspicion of severe rise of intracranial pressure. Increasing drowsiness is another important sign. In some posterior fossa tumours the first sign indicating urgency may be the onset of rapid, bubbly and laboured breathing without any loss of consciousness, but usually with severe dysarthria. The emergency methods of reducing raised intracranial pressure in these cases are as follows.

(1) Hypertonic solutions

Intravenous hypertonic solutions (50 per cent glucose, or 15 per cent sodium chloride, in amounts of 50 to 100 cubic centimetres for an adult) can be used to reduce raised intracranial pressure in an emergency, but they have a temporary effect only and are not successful when the rise of intracranial pressure is localized and due to cerebral oedema and herniation. The method is useful in temporarily reviving a patient with hydrocephalus admitted to hospital in coma and showing papilloedema. After an intravenous injection of hypertonic solution such a patient will often respond sufficiently to co-operate in a clinical examination, but operative treatment, often necessarily preceded by ventricular estimation or ventriculography, should follow without delay.

In the pre-emergency phase of raised intracranial pressure, when consciousness is still unimpaired but headaches are severe, hypertonic solutions may be given per rectum if for any reason operative treatment must be delayed. Magnesium sulphate crystals (3 ounces in 3 fluid ounces of water) should be instilled through a high rectal tube and should be retained as long as possible.

(2) Ventricular drainage

This may tide a patient over a dangerous period while a localizing diagnosis is being made. A ureteric catheter or fine polythene tube is passed into the lateral ventricle through a burr hole, and cerebrospinal fluid is allowed to drain away at a pressure of 150–200 millimetres of water (Fig. 254). The tube may be left in place for several days and then be used for air injection and ventriculography immediately before operation.

(3) Operation

In most cases the best emergency treatment is a direct attack on the tumour by open operation. Patients drowsy from raised intracranial pressure will

usually withstand a careful ventriculography or arteriography, provided a radical operation follows immediately the x-ray films are developed. In cases of doubt, ventricular estimation may give all the additional diagnostic information that is required.

The higher the intracranial pressure the greater is the need for fairly radical relief. To avoid the further rise of intracranial pressure which accompanies general anaesthesia, local anaesthesia should be used. Particular care is required in haemostasis of the scalp and deep layers because of the pronounced tendency to bleeding until intracranial pressure is reduced. The objective in these operations is a slack brain with cerebrospinal fluid flowing freely at the former site of obstruction. Removal of the tumour will usually accomplish

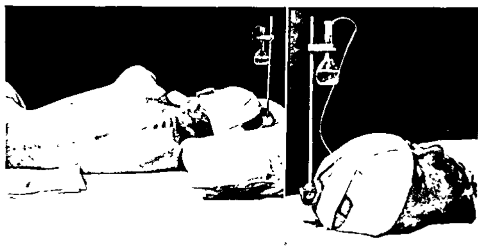


FIG. 254.—Ventricular drainage. A fine polythene tube has been put into the anterior horn of the right lateral ventricle and drains at positive pressure into a flask mounted on a rotating stand which is attached to the patient's head. Note also that in this case there is an indwelling polythene tube in the lumbar subarachnoid space.

this, but there are some cases of temporal lobe tumour or abscess in which it is also necessary to remove adjacent oedematous white matter, in order to disimpact the herniated hippocampal gyrus from the tentorial opening, before cerebrospinal fluid will run freely again. In a superficial vascular meningioma it may suffice to divide completely the dural attachments of the tumour, leaving the extirpation for a second stage when the cerebral venous pressure is not so high, and the patient is in better condition to withstand blood loss.

When symptoms of severe rise of intracranial pressure supervene lives will be saved by prompt operative measures. Even after the patient has stopped breathing operation may be proceeded with under artificial respiration, but unless the patient begins to breathe spontaneously after relatively minor operative procedures, such as ventricular tap, decompression of the foramen magnum, or aspiration of a cystic tumour, he rarely recovers. Neurosurgical clinics must be so organized as to be able to undertake promptly all the diagnostic and therapeutic operative procedures which are required in dealing with urgent cases of raised intracranial pressure.

3. SURGICAL PRINCIPLES IN CEREBRAL OPERATIONS

(1) Adequate exposure

Adequate exposure is most important: a few millimetres additional exposure in one direction or another may render easy an operation which would otherwise be extremely difficult. There are few routine exposures—the sub-occipital operation to expose the posterior fossa, the transfrontal exposure of the chiasmal region—and even these may be modified with advantage when large or

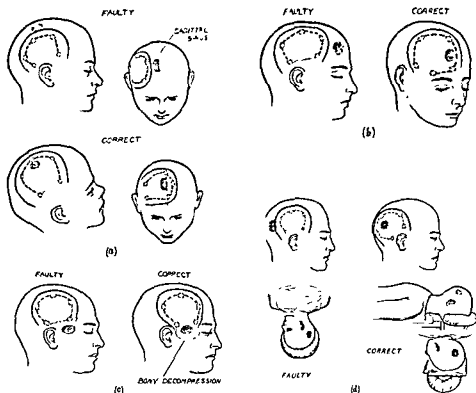


Fig. 255.—Examples of faulty and correct scalp and bone flaps for exposure of tumours of the cerebral hemisphere. (a) Parasagittal tumour; (b) prefrontal tumour; (c) anterior temporal tumour; (d) occipital tumour; for this exposure the patient should lie prone on the operating table, either face down or with his face turned towards the side from which the tumour is to be removed.

unusually situated tumours have to be removed. In all other cases the incision, both of the scalp and skull, should be planned for each individual case. Examples of adequate and of faulty exposures are shown in Fig. 255 (a), (b), (c) and (d). *Planning of incision*

For the surgeon, accurate localization of most brain tumours depends in the first instance upon recognition of disordered function of some part or parts of the brain, then on the conversion of this "physiological" diagnosis into a topographic anatomical diagnosis. This process of clinical localization should, whenever possible, be checked by direct visual evidence, such as can be obtained from skiagrams or from ventriculography and arteriography. Visual evidence is all the more important because a tumour may originate in a

silent area and only produce localizing symptoms when its growing edge approaches one of the more "eloquent" areas of the brain. With all these aids to diagnosis considerable errors in operative exposure may still arise.

As a general rule bone flaps should be on the large side. For example, with a tumour attached to the sagittal sinus a bone flap which crosses the middle line greatly facilitates the exposure (Fig. 255 (a)) and also enables the surgeon to work outside the boundaries of the tumour, thus lessening the blood loss.

Cerebro-cranial topography

The details of cerebro-cranial topography which are customarily taught are of little value. It is essential for the surgeon to have an accurate conception of the position of the lateral ventricles (Fig. 240) so that he may tap them from any part of the exposed brain, and with the head in any position. The Sylvian fissure lies at a much higher level in the cranium than would seem likely from its origin on the ventral surface of the brain; it cannot normally be exposed through a subtemporal decompression and only comes into view during that operation if it is displaced downwards by a frontal tumour. The Rolandic fissure lies rather far back on the convex surface of the cerebral hemisphere, usually about 2 to 3 centimetres behind the main anterior meningeal channel in the parietal bone. At necropsy it can be readily recognized by its great depth, but in life it can only be identified with certainty by electrical stimulation of the precentral gyrus. Tumours which first involve the leg area of the precentral gyrus are likely to be presenting as much on the medial as on the lateral surface of the cerebral hemisphere, and the area for the hand is a wide one and extends close to the middle line.

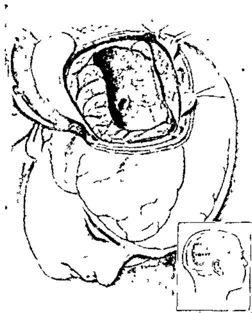


FIG. 256.—To illustrate the exposure for occipital lobe tumour. A large oligodendroglioma has been removed; the ventricle has been opened.

The geniculo-calcarine pathway traverses a large part of the cerebral hemisphere, and there is no certainty of easy operative exposure of a tumour which produces complete homonymous hemianopia. When homonymous hemianopia is known to begin in the lower quadrants there is a strong likelihood that the tumour is occipital, or occipito-parietal, rather than temporal, and the surgeon should so plan his bone flap as to expose all the brain between the occipital pole and the Rolandic fissure (Fig. 256). Tumours in which the initial symptom is a complete homonymous hemianopia have an unfortunate habit of being on the inferior surface of the temporal lobe and are usually difficult to expose.

Meningiomas of the anterior fossa, arising from the olfactory groove and the sphenoidal ridge, are approached through a frontal flap, but often can only be exposed by resection of part of the overlying frontal lobe. Usually

only a small part of the frontal pole need be removed (it is incorrect to describe this as lobectomy) and whatever symptoms may result from sacrifice of this normal brain tissue are usually more than balanced by the improvement in brain function which results from successful removal of the tumour. When resecting frontal convolutions in the dominant hemisphere it is important to keep away from the Sylvian fissure in order to avoid damaging speech function. For a similar reason, when approaching a deep temporal tumour in the dominant hemisphere it is necessary to avoid the superior temporal convolution and to incise the temporal lobe either through the middle or inferior temporal convolutions.

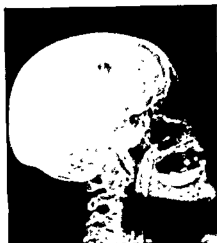


FIG. 257.—Blocked intratracheal tube.

Third-ventricle tumours blocking the foramina of Monro can be exposed through an opening into the anterior horn of the lateral ventricle (Fig. 252). If the ventricle is already considerably dilated this exposure is easy, but if the hydrocephalus is inconsiderable the exposure may be very difficult, and before making the transventricular approach it is usually wiser to do a preliminary osteoplastic decompression of the frontal lobe and allow the anterior horn to dilate further, as it will do in the presence of obstruction within a few months.

(2) The management of raised intracranial pressure and brain swelling during operation

When intracranial pressure is high, venous pressure in the scalp, skull, dura and brain is also usually raised, with the result that the tendency to haemorrhage from large and small veins is greatly increased. When the dura is opened the brain may bulge out to an alarming extent and the cortex may split open with bleeding from many cerebral vessels. Such events may wreck an operation, leading to death from blood loss, or to profound impairment of function should the patient survive. These risks from operating when intracranial pressure is high can be avoided by attention to the following principles.

(*a*) *Avoidance of further rise of intracranial pressure*

Rise of venous pressure is the commonest cause of further rise of intracranial pressure during operation. General anaesthesia produces such a rise, and probably the main way in which it acts is by obstruction to respiration. Anything which interferes with free inspiration and expiration causes rise of intracranial venous pressure and further brain swelling—for example, a blocked or partially blocked airway, as from the tongue falling back, or from an ill-placed, an over-small or a partly blocked intratracheal tube (Fig. 257). Free expansion of the thorax in inspiration aspirates blood from the cranium; impeded inspiration not only results in damming up of blood in the cranium but also, since the carbon dioxide content of this blood rises, produces dilatation of the cerebral capillaries and thus further brain swelling. This

Rise in blood carbon dioxide

power of carbon dioxide to raise intracranial pressure can be shown by the effect of inhalation of air containing excess of carbon dioxide on the manometric pressure of the lumbar cerebrospinal fluid (Fig. 258). Shallow respiration after a full dose of morphine is also associated with a rise of intracranial venous pressure and of ventricular pressure which can be overcome if the patient can be roused to breathe deeply.

Therefore in patients with severe rise of intracranial pressure the following rules are useful.

(i) Avoid general anaesthesia when possible; operate instead under local anaesthesia, at least until the tumour is removed and all danger from raised intracranial pressure is at an end.

(ii) At all times during operation maintain a free airway (this rule should apply in all intracranial operations, whether under general or local anaesthesia).

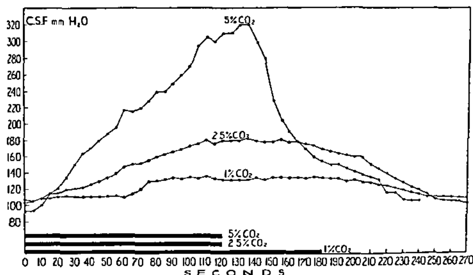


Fig. 258.—The effect of inhalation of CO_2-O_2 mixture on intracranial pressure, as measured by spinal manometry.

(iii) Avoid morphine, except in small doses ($\frac{1}{8}$–$\frac{1}{6}$ grain).

(iv) Never use carbon dioxide mixtures to stimulate breathing, either during general anaesthesia or at other times.

Intracranial pressure may be raised by obstruction to the veins of the neck, by pressure of any object upon the jugular veins. Extreme lateral rotation of the head may also obstruct one internal jugular vein.

Lowering the head tends to increase intracranial venous pressure, and raising it has the reverse effect. In the sitting position intracranial pressure is considerably lower and venous bleeding is less: large venous sinuses, such as the cavernous and superior longitudinal sinuses, bleed little when then opened, or not at all. The sitting position is therefore of considerable value in those intracranial operations in which it can be safely employed.

(b) Reduction of intracranial pressure by withdrawal of cerebrospinal fluid

The use, intravenously, of hypertonic solutions is rarely of much value to reduce severe rise of intracranial pressure during operations. A much more

effective method is to remove cerebrospinal fluid from the ventricles or from the large cisterns. As a general rule the surgeon should ensure that the ventricular system is always accessible during intracranial operations. In posterior fossa operations the posterior horns of the lateral ventricles should be tapped (Fig. 259). In operations upon one hemisphere the corresponding lateral ventricle is usually collapsed and therefore when draping the patient's head provision should be made to obtain access to the opposite lateral ventricle which is usually dilated (Fig. 259).

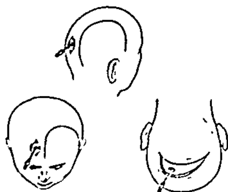


FIG. 259.—Reduction of intracranial pressure by tapping the lateral ventricle during intracranial operations.

Intracranial pressure is not always the same in all compartments of the cranial chamber. This is often demonstrated in operations for tumour of the posterior fossa, when, no matter how much cerebrospinal fluid is aspirated from the lateral ventricles, the pressure in the posterior fossa remains high and the cerebellum bulges back strongly as its overlying dura is opened. In such cases prompt relief of the raised pressure in the posterior fossa is obtained by evacuating the cerebrospinal fluid from the cisterna magna: the cerebellum will sink back as much as 1·5 centimetres and it is easy to proceed with the operation. It might be thought that posterior fossa pressure could be reduced immediately before operation by lumbar drainage, but such a manoeuvre would encourage further herniation of the cerebellar tonsils through the foramen magnum and might thus produce fatal medullary compression. Lumbar puncture is indeed highly dangerous in raised intracranial pressure, and as a general rule, in patients with high papilloedema, severe headache, vomiting and drowsiness, it should only be done, if at all, on the threshold of the operating theatre.

(c) *Reduction of raised intracranial pressure by removal of the tumour*

The steps so far recommended to reduce raised intracranial pressure have only temporary effect. Removal of the tumour is the only certain way of obtaining more than temporary relief. No matter how much cerebrospinal fluid may have been previously withdrawn from the ventricles or cisterns much fluid escapes as a tumour is removed, from such bottle-necks as the fourth ventricle and aqueduct of Sylvius, the Sylvian fissure, or the medial surface of the cerebral hemisphere.

(3) Avoiding injury to the brain

In removing large encapsulated tumours, cysts or abscesses the surrounding brain may be seriously injured unless the volume of the expanding lesion is reduced. Cysts or abscesses can be aspirated (Fig. 260), and solid tumours can usually have their interior gutted with pituitary rongeurs or the endothermy loop (Fig. 261). The surrounding brain can then be gently brushed away from the capsule of the lesion, and such firm retraction as is required can be exerted against the tumour instead of against the brain. This method *Reducing mass of tumour*

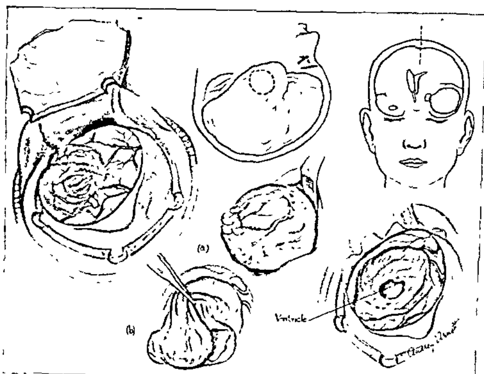


FIG. 260.—Removal of left temporal brain abscess. The abscess was very large and was buried in the brain substance. In order to avoid heavy retraction of the brain substance, and to accomplish the deep parts of dissection under direct vision, the abscess (a) was emptied (b); the later stages of the excision were thus rendered easy and less dangerous.

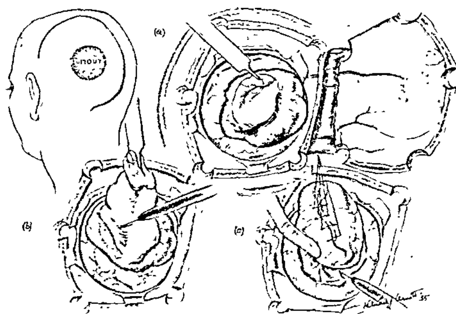


FIG. 261.—A left occipital meningioma. After the superficial part of the tumour had been exposed (a) a large section of it was removed by diathermy needle (b) and the remaining part was stitched up. The reduced mass was then removed without damage to the surrounding brain (c).

is invaluable in avoiding injury to the brain, particularly in those large ovoidal meningiomas which lie mainly concealed by brain substance. Moreover, repeated gutting of the interior of such a tumour facilitates exposure of the blood-vessels which so often lie beneath the tumour; rupture of one of these vessels while the depths of the tumour bed are still obscured by a large overlying mass of tumour may be catastrophic.

Exposure is in fact obtained at the expense of the tumour rather than at the expense of the surrounding brain. In opening the dura to expose a surface tumour it is desirable to limit the opening, so far as possible, to the site of the tumour in order to avoid herniation of the adjacent healthy brain. Such herniation is in itself damaging to the displaced convolution and it also renders exposure of the tumour more difficult.

Limitation of dural opening

Whenever the surface or the substance of the brain must be retracted for any length of time it should be protected with a strip of sheet gutta-percha covered by a strip of lintine (Fig. 252). Violent retraction not only may start subpial, subarachnoid and intracerebral haemorrhage, as well as lacerating the brain, but in cases of severely raised intracranial pressure it may set up acute brain swelling. This condition appears to consist primarily of an acute dilatation of all the cerebral capillaries: the whole of the exposed brain swells to a remarkable extent and bleeds from all parts. So great is the swelling that it is almost impossible to close the wound, and removal of brain tissue is only followed by the protrusion of more. Acute brain swelling is usually seen only in unfavourable cases — malignant tumours with severe rise of intracranial pressure—but we have seen it after prolonged and severe retraction of the temporal lobe during removal of a deep temporal meningioma.

Acute brain swelling

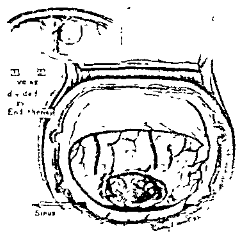


FIG. 262.—Division of cerebral veins during removal of a small left frontal parasagittal meningioma. After operation the patient developed motor and sensory paralysis of the right upper limb and aphasia, which recovered completely in about 3 weeks. This complication is attributed to interference with venous return from the lateral parts of the left hemisphere.

The brain can be damaged during operation by division of important arteries and veins. When benign tumours lie in contact with the anterior or middle cerebral arteries there may be considerable risk of dividing these vessels, thereby leaving the patient maimed for life though the tumour has been removed. In such cases the process of whittling away the mass of the tumour by repeated gutting of its interior is useful, so that when the main arteries are being approached there is room to identify them, and the surgeon can decide deliberately whether it is safe to remove the whole of the tumour capsule or better to leave a small fringe of tumour attached to the artery.

The parts of the brain in and around the bed of a tumour are vulnerable to

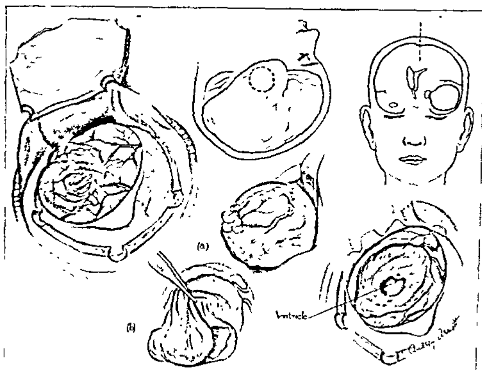


FIG. 260.—Removal of left temporal brain abscess. The abscess was very large and was buried in the brain substance. In order to avoid heavy retraction of the brain substance, and to accomplish the deep parts of dissection under direct vision, the abscess (a) was emptied (b); the later stages of the excision were thus rendered easy and less dangerous.

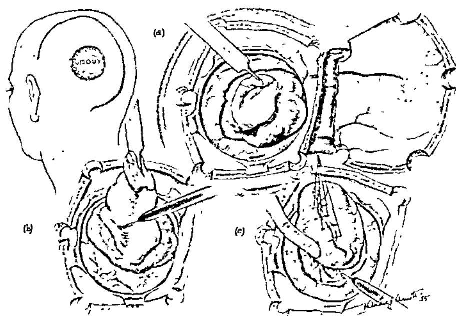
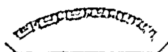
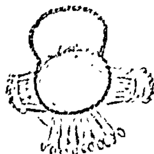


FIG. 261.—A left occipital meningioma. After the superficial part of the tumour had been exposed (a) a large section of it was removed by diathermy needle (b) and the remaining part was stitched up. The reduced mass was then removed without damage to the surrounding brain (c).

In a long intracranial operation these methods of scalp haemostasis may be too effective; part of the scalp may be rendered so anaemic that its edge subsequently undergoes necrosis (Fig. 265). Therefore, once the surgeon finds that removal of the tumour will take a long time, his first step should be to re-examine the scalp wound, and to remove or lighten the hold of any forceps or clips which look likely to cause anaemic necrosis of the scalp.

Avoidance of anaemic necrosis





Sutures

FIG. 264. Reflection of scalp flap. On the flap side haemostasis is obtained by spring clips (*see also Inset*); on the other side by forceps.

Because of the fibrous septa of the scalp it is not possible to ligate the scalp vessels, with the exception of such main vessels as the *superficial* temporal and occipital arteries. Therefore *during closure, haemostasis of the scalp is* obtained by sutures (*see below, under* Wound closure).

(b) *Skull*

Bleeding from diploic vessels and emissary veins can be very severe, and the only satisfactory method of stopping it is to block the openings in the bone with some paste-like material. Horsley's wax (yellow beeswax 3 parts and castor oil 1 part, sterilized in an electric oven at 350° F. and stored in *1 in 1,000 mercuric chloride* solution) is very satisfactory for this purpose. It should not be used too vigorously in stopping large emissary veins, for the wax may be pushed or carried into the main venous sinuses. We have once seen at necropsy, after a posterior fossa operation, a pulmonary embolus which contained a small ball of wax in its centre.

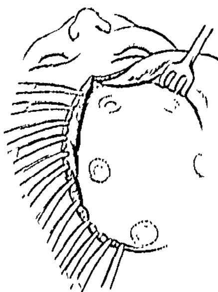


FIG. 265.- Constriction of scalp vessels in wound edge by clamps attached to galea aponeurotica. If prolonged this may cause necrosis of scalp edge.

Bleeding from diploe

While a bone flap is being cut by a *Gigli saw much blood may be lost* both from cut diploic channels and from meningeal veins. The diploic channels may be stopped by waxing the saw cuts. The meningeal veins bleed when the dura is separated from the bone, and there is no way of directly stopping these bleeding points until the bone flap is raised. *However, the dural veins will stop* bleeding as soon as the guide which displaces and protects the dura during the saw cut is removed (Fig. 266). Saw cuts should therefore be done speedily if the bleeding is severe.

interference with their venous drainage. A meningioma alongside the sagittal sinus frequently displaces the cerebral veins which are draining into the sinus. One or more of these veins may lie in front of or behind the tumour (Fig. 262), and if they are divided in the course of removing the tumour the patient may develop hemiplegia, with or without aphasia, in the first few days following the operation. These symptoms, fortunately, usually clear up spontaneously, but probably not without leaving some permanent damage, such as a greater tendency to post-operative epilepsy than would otherwise exist. Therefore, whenever possible, the main cerebral veins round a tumour should be conserved.

Risk of hemiplegia

(4) Haemostasis

Before modern neurosurgical technique was developed many deaths after operation for intracranial tumour were due to blood loss, or to compression of the brain by blood clot. All the tissues traversed during operation—the scalp, skull, dura mater and brain—are normally very vascular, and when there is an intracranial tumour they tend to become excessively vascular. Rise of intracranial pressure causes venous engorgement of all the tissues and sometimes a rise of arterial pressure. Most brain tumours have a rich blood supply and bleed easily, and those which are attached to the dura usually cause great hypertrophy of the blood-vessels of the neighbouring dura and of the overlying bone.

Hypertrophy of blood-vessels

Patients with brain tumours withstand blood loss badly. They may die upon the operating table, or be left with such a small amount of haemoglobin that they are unable to overcome other post-operative complications, such as wound infection and aspiration pneumonia. Haemostasis therefore is one of the main preoccupations of the neurosurgeon. The methods used in preventing blood loss vary with the different tissues.

(a) *Scalp*

To prevent blood loss during the initial stage of the operation, the incision is first outlined with a scratch and the scalp is compressed on either side as the incision is being made (Fig. 263). The deep layers of the scalp contain numerous fibrous septa which prevent the cut blood-vessels from retracting, and render it difficult to grasp each vessel with haemostatic forceps. The only satisfactory way to obtain haemostasis is to compress the whole of the cut edge of the scalp, either by applying haemostatic forceps to the galea aponeurotica at regular intervals and thus drawing the galea under tension over the more superficial layers of the scalp, or by applying spring clips to the whole thickness of the scalp (Fig. 264). Compression of the scalp against the underlying bone should be maintained until forceps or clips have been applied. With these methods a large incision can be made in the scalp with practically no blood loss.

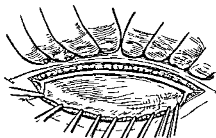


FIG. 263.—Haemostasis of scalp; digital compression, followed by application of haemostats to galea.

the cerebral hemisphere, or is attached to the base of the skull, the source of the tumour's blood supply can only be dealt with at a late stage of the extirpation, and that is one reason why removal of such tumours may be difficult.

Meningiomas are usually suitable for gutting by endothermy, a procedure which greatly facilitates the removal of the remaining shell. If the interior of the tumour is vascular the ability to carry out this manoeuvre may depend upon finding the right strength and quality of endothermy current to deal with the bleeding points, but much may be done by firm compression with pledgets of wool, or of the collapsed superficial parts of the tumour against the bleeding points.

(e) Irrigation and suction

Throughout intracranial operations bleeding points are displayed by means of suction, sometimes assisted by irrigation with Ringer's solution. While the sucker is useful, in fact indispensable, for this purpose its excessive use, particularly in the neighbourhood of large bleeding veins, may encourage bleeding, which could be controlled easily by pressure, and may result in the loss of large quantities of blood.

(f) Prophylactic intravenous transfusions

Whenever there is likely to be much blood loss it is wise to set up an intravenous drip in a saphenous vein at the beginning of the operation. There should be no hesitation in giving blood. For the removal of a large vascular meningioma as much as 4 or 5 pints of blood may be required. It can be given rapidly or slowly, as bleeding from the operative field is rapid or slow. If the patient's systolic blood-pressure can be prevented from falling below 100 millimetres Hg the post-operative course is usually smooth. If for want of blood the patient's systolic pressure falls to 60 or 70 millimetres Hg the peripheral vessels may contract so that it is impossible to get the blood into the patient. This is a serious state of affairs. The operation cannot proceed until the transfusion is running.

Contraction of peripheral vessels

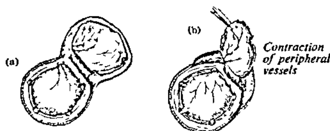


FIG. 267.—(a) Old method of reflecting an osteoplastic flap; the bone flap was left attached to the overlying scalp as well as to the temporal muscle. (b) Newer method: the scalp and bone flaps are reflected separately.

(g) Avoiding post-operative clot

Before the wound is closed haemostasis should be meticulous. No doubtful point of oozing in the tumour bed should be left without a patch of fibrin foam. At this stage the brain should be quite slack and any bulging should arouse suspicion of deep-seated concealed bleeding (or of respiratory obstruction). The subdural space should be cleared of clot.

Extradural bleeding

Extradural bleeding is most to be feared, for it can cause death within 24 to 48 hours after operation. Its incidence used to be as high as 5–10 per cent in the days when the bone flap was left attached to the scalp (Fig. 267), but now that we have found that the bone flap can survive quite satisfactorily

All venous bleeding from bone and dura is worse when intracranial pressure is high. It can usually be reduced by withdrawing cerebrospinal fluid from the lateral ventricle.

(c) *Dura mater*

The methods of stopping vessels of the dura mater are largely those employed in the brain (*see below*), but special methods are employed during closure to prevent post-operative extradural clot.

(d) *Brain*

Most of the sizable vessels of the brain lie on its surface, in the subarachnoid space. They cannot be grasped with haemostatic forceps and ligated as in other parts of the body, since they lack the support of connective tissue which makes that procedure possible. The methods employed are, for the larger arteries and veins, silver clips, and for the smaller vessels endothermy, both methods introduced by Cushing.

Silver clips
Endothermy

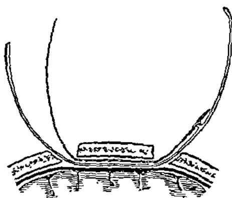


Fig. 266.—Separation of dura from skull by passage of a Martel guide and Gigli saw.

For small oozing points in the brain substance, holes in the large venous sinuses, or severe bleeding from deep parts which cannot be sufficiently well exposed to display the bleeding points, haemostasis is best obtained by the application of some clotting agent. Cotton-wool pledgets (after immersion in Ringer's solution), firmly applied and left for several minutes, are often effective in stopping mild haemorrhage; for severe or persistent bleeding a fragment of temporal or complexus muscle, beaten out flat, used to be employed, but has now been superseded by fibrin foam soaked in thrombin solution or by oxidized cellulose gauze.

Fibrin foam
Oxidized cellulose gauze

Bleeding from tumours is dealt with in much the same way as bleeding from the brain, but the endothermy is usually more freely used since the burning of the surrounding tumour tissue does no harm, and is in fact an advantage. Bleeding is always less if the surgeon can dissect outside the tumour margin instead of removing the tumour piecemeal. This is best exemplified in solid cerebellar haemangioblastomas, which bleed fearsomely if opened, but can be removed with practically no bleeding if a fringe of the surrounding cerebellar tissue is removed with them. In such cases the ability to carry out a total extirpation bloodlessly depends upon obtaining a really adequate exposure.

Raised intracranial pressure increases the liability to bleeding from the vessels of the tumour. Hence it may be desirable to tap the lateral ventricle before starting to remove the tumour. Local rise of intracranial pressure in the vicinity of the tumour is best dealt with by complete encirclement of the surface attachments of the tumour, whether they be dual, arachnoidal or cerebral, at the earliest possible stage. Then the tumour can begin to extrude and local pressure falls. This manoeuvre also tends to reduce the blood supply of the tumour, since most of that comes from the surface of the brain or from its membranes. When a tumour presents on the inferior or medial surface of

prevented by interposing a sheet of gutta-percha, or better still fibrin film, between the brain and overlying temporal muscle or bone.

After careful haemostasis the bone flap is replaced. Some surgeons fix it with tantalum or stainless-steel wire, but we have found that it is satisfactorily held in place by stitching the pericranium in a few places. *Pericranium stitched*

The most important part of the closure is suture of the scalp. The requirements are (a) haemostasis of the scalp; (b) linear approximation of the skin edges without undue tension so that perfect first-intention healing is obtained and the wound is in such a good state that it could be reopened if necessary within the next few days without risk of sepsis; and (c) that the approximation is secure enough to prevent leakage of cerebrospinal fluid in the first few days, and spreading of the wound edges if later the flap is subjected to raised intracranial pressure.

The most effective method, probably the only method, of obtaining satisfactory wound healing after operations for intracranial tumour is to close the scalp in two layers—a buried layer of interrupted stitches through the galea aponeurotica, and a superficial layer of stitches approximating the skin edges (Fig. 270). All the tension is taken by the buried stitches; the superficial stitches are merely for approximation of the epithelial edge and should all be removed within 4 days. Fine silk is used throughout. It is sterilized in Horsley's wax at 350° F. and is kept in mercuric chloride solution (1 in 1,000). *Two-layer closure of scalp*



Fig. 270.—Scalp closure.

In operations upon the posterior fossa it is important to obtain a firm closure of the occipital muscles at the superior curved line, otherwise there is risk of a leak or of a subcutaneous bag of cerebrospinal fluid.

(6) Avoiding infection

The risks of infection at intracranial operations are considerable. Bacteria which are not pathogenic in most parts of the body can set up meningitis which either is fatal or produces chronic hydrocephalus with perpetuation of symptoms. The ventricles and the large basal cisterns seem to be more vulnerable to entering bacteria than is the brain itself, with its rich supply of microglia. Any superficial infection of the wound, such as a stitch abscess, will interfere with healing and so increase the risk of cerebrospinal fistula, and will also completely undo plans for a two-stage removal of a tumour. *Chronic hydrocephalus*

The sources of infection of operation wounds are those usual to all operations—bacteria in the air of the operating theatre, including those from the noses and throats of the operating staff; bacteria from the hands of the staff, through holes in gloves; bacteria from the scalp of the patient, from suture material, from instruments and also from the lotions used for irrigation of the operative field. *Sources of infection*

Neurosurgical operating theatres should not be used for other purposes. They should be air-conditioned and all the methods of eliminating bacteria from the various sources should be subject to systematic regular tests by a bacteriologist. With all these precautions it is still impossible to eliminate bacteria from the wound. We have found that a powder of Sulphamezathine with penicillin (5,000 units per gramme) insufflated into the various layers of the wound before closure has significantly reduced our incidence of *Sulphamezathine-penicillin powder*

with no other attachment than temporal muscle and pericranium, the scalp flap and the bone flap are turned separately. The inner surface of the bone tends to ooze less, and, what is probably more important, there is ample room in the subgaleal plane for blood escaping from the extradural space. As a result post-operative clot, although it has not been abolished, has become rare.

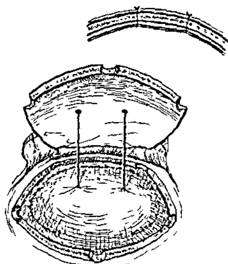


FIG. 268.—Stitching dura to pericranium to prevent post-operative extradural haematoma. (*After Poppen.*)

The dura is usually very vascular and may tend to bleed from many points. These may be treated with patches of fibrin foam or by endothermy, but sometimes the only way to stop the bleeding is to divide the dura round the greater part of its exposed surface, then stitch it up again. Another method of preventing extradural clot from an oozing dura is to obliterate the extradural space by stitching the dura to the pericranium through holes in the skull (Fig. 268). Bleeding from beneath the bone edge can be stopped by stitching the dura to the pericranium (Fig. 269).

Clouding of consciousness

The main symptom of post-operative extradural clot is a progressive clouding of consciousness. Within from 4 to 24 hours after the operation the patient ceases to respond promptly and becomes increasingly difficult to rouse. This state may be preceded by a phase of violent restlessness. The pupil on the side of operation tends to become dilated and sluggish in its reaction to light, and there may be weakness of the contralateral limbs. The eyelids tend to swell and close unusually early and the scalp flap becomes shiny and tight. The pulse may be slowed and the blood-pressure raised.



FIG. 269.—Control of extradural bleeding from beneath the bone edge by stitching dura to pericranium.

Post-operative clot is highly dangerous. When there are reasonable grounds for suspecting its presence the wound should be reopened without delay and the clot should be scraped off the dura. It is rare to find any single bleeding point. If the dura continues to ooze it should be devascularized by dividing most of its circumference, and then it should be stitched up again.

Devascularization of dura

(5) Wound closure

It is not always possible to close the dura completely, and indeed it is sometimes desirable to leave part of it open over a silent area of the brain, to form a decompression. The cortex is damaged by being deprived of its dural covering, though usually no symptoms result from this damage or from adhesion of the temporal muscle to the cortex. However, the adhesions can be

Over-all operative mortality for intracranial tumours will depend to some extent upon the surgeon's attitude, which can vary between the excessively radical and the excessively cautious. It is not easy to maintain a middle course, but a continuous critical examination of results, in terms of the symptomatic relief afforded to the patient and its effect upon his working capacity, is the surgeon's best guide. There is no valid reason why a neurosurgical clinic should have a case mortality of more than 10 per cent, and it is doubtful whether any clinic could sustain a higher mortality for long without serious loss of morale of all concerned.

6. RADIATION THERAPY

Once the rise of intracranial pressure has been relieved x-ray therapy may be very useful in certain types of case. Cerebellar medulloblastoma is the most radio-sensitive of the intracranial tumours, and as it is prone to metastasize the treatment should be applied to the whole central nervous system.

Other malignant gliomas show a varying, to some extent unpredictable, response to radiation therapy. The results are often disappointing, but are on occasions so satisfactory as to render the method worthy of trial in all irremovable gliomas in which brain function is reasonably well preserved. Most tumours of the pineal region are better treated by a short-circuiting operation and x-ray therapy than by direct operative attack upon the tumour; the functional results are better.

I have found that some meningiomas are sensitive to x-rays and after doing a decompression have irradiated the very large vascular tumours, as a prelude to removing them at a later stage.

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[References to other titles are given under Brain—Tumours and Technique in the Index Volume. The subject of Brain Tumour is also dealt with in the *British Encyclopaedia of Medical Practice* (1936), Vol. 2, p. 619.]

post-operative sepsis. We use 1–2 grammes of this powder per case—lightly frosting the tissues with it—and the fluids in the wound have been found to contain a bacteriostatic concentration of penicillin for about 18 hours. It is important not to use sulphathiazole instead of Sulphamezathine as it is highly convulsant when applied to the brain.

Sulphathiazole contra-indicated

4. AFTER-CARE

Sedatives

Restlessness in the first 24 hours after operation can usually be allayed by chloral and bromides by mouth or rectum. Morphine is sometimes required but should only be given in small doses (⅛ grain or less) for fear of masking the symptoms of post-operative clot.

Prevention of aspiration pneumonia

In the first days after operation particular care is often required to prevent aspiration pneumonia. Swallowing may be interfered with by drowsiness, by hemiplegia, or after posterior fossa operations by direct damage to its reflex pathways. Not only fluids ingested, but also mucus from the mouth and naso-pharynx, which may sometimes be excessive, may pass into the trachea and set up pneumonia. The patient's powers of swallowing should first be tested in the horizontal semi-prone position, so that, if he cannot swallow, the fluid trickles out of his mouth. Feeding can be effected by stomach tube. If the mucus is troublesome and the patient's respiration tends to become bubbly and laboured the foot of his bed should be raised, in spite of the fact that this raises intracranial pressure.

Daily dressings

Care of the wound requires that dressings should at first be done daily. Excessive tension on the wound may be due to subcutaneous collections of blood and cerebrospinal fluid which can be relieved by needling and aspiration of the wound, or to post-operative cerebral oedema which should be treated by lumbar puncture and withdrawal of cerebrospinal fluid.

Hyperthermia

Hyperthermia may follow operations upon the brain stem, especially in the region of the floor of the third ventricle. To prevent its onset the patient should be lightly clad once he has recovered from the low temperature which is usually present immediately after a prolonged intracranial operation. For treatment of hyperthermia of over 105° F. (rectal) a rectal drip of iced water and small doses of morphine are probably as good as anything.

Physical re-education

In most cases when an intracranial tumour has been completely removed convalescence is smooth and rapid, and soon the patient can be started upon his physical re-education—massage, and active and passive movements in cases of recovering hemiplegia, and graduated exercises of a general character in those who are not paralysed. All paralysed limbs should be passively stretched through their full range of movements once a day to prevent contractures and adhesions.

There is not often need for active re-education of speech or sight, for after an intracranial tumour has been removed these functions usually recover spontaneously and rapidly if they are going to recover at all.

5. OPERATIVE MORTALITY

With improvements in diagnosis and operative technique the common causes of death—haemorrhage, sepsis, and shifts of the brain from operating in the wrong place—have been greatly reduced though by no means eliminated.

opening on the surface of the nipple, of its branches, and of the acini which develop at the inner extremity of each terminal branch. The connective tissue surrounds and supports the glandular elements, the whole forming the corpus mammae which lies in the superficial fascia of the chest wall.

The breast tissue is not enclosed in a true capsule. It is not attached to the pectoral fascia on which it lies, but is attached to the overlying skin by the suspensory ligaments which, arising from the superficial fascia enclosing the breast, traverse the subcutaneous fat and are attached to the deep layers of the skin. Lymphatic vessels accompany the ligaments.

Anatomical relations

The anatomical limits of the breast tissue are: superiorly, the level of the second rib; inferiorly, the sixth costal cartilage; medially, the lateral border of the sternum; and laterally, the mid-axillary line. The axillary tail (Spence) is a narrow prolongation of the breast upwards towards the axilla under the edge of pectoralis major. In its upper half the breast lies on the pectoralis major muscle, the pectoral fascia intervening; in its lower half, medially, on the external oblique aponeurosis where it covers the upper part of the rectus abdominis muscle, and, laterally, on the serratus anterior muscle and the digitations of origin of the external oblique.

Arterial supply

The arterial supply of the gland is from the lateral thoracic branch of the axillary artery, which runs downwards and medially along the lateral border of pectoralis minor, and from the anterior perforating branches of the internal mammary artery which pass forwards through the medial ends of the upper intercostal spaces and reach the gland by penetrating pectoralis major near the margin of the sternum.

Lymphatic drainage

The lymphatic vessels of the breast are arranged as follows. Plexuses of small lymph vessels lie round the acini and communicate with the sub-areolar plexus by vessels passing along the ducts. From the peri-acinous plexuses lymph is also carried to lymphatic vessels on the anterior and posterior surface of the gland. From the latter, and from the sub-areolar plexus, the larger lymphatic channels run to the regional lymph glands. The main line of drainage runs laterally to the axilla, the pectoral and subscapular groups of glands being the chief recipients. Lymphatics from the medial part of the breast drain medially into channels which pass into the mediastinum alongside the anterior perforating arteries and enter the anterior mediastinal lymph glands. From the upper part of the breast lymph vessels may pass directly over the clavicle to the supraclavicular glands. From the lower part of the breast lymph vessels pass downwards and communicate with the sub-diaphragmatic extraperitoneal plexus, while from the medial part some lymph channels pass across the midline to join the lymphatic plexus of the opposite breast.

Axillary lymph glands

As the axillary lymph glands receive most of the lymphatic drainage, they are the most important surgically. They are arranged as follows: (1) pectoral group, lying under the edge of pectoralis major along the line of the lateral thoracic vessels; (2) subscapular group, lying along the subscapular vessels on the subscapularis muscle; (3) lateral group, lying along the axillary vein (not draining the breast directly); (4) apical glands, at the apex of the axilla behind the costo-coracoid membrane, lying in relation to the first intercostal space and the upper part of the axillary vein: they receive efferents from the three previous groups, and also from (5) the infraclavicular glands in the superficial

BREAST—CARCINOMA OF

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1. ANATOMY

Corpus mammae

77.] The breast consists of glandular tissue of ectodermal origin and supporting connective tissue of mesodermal origin. The glandular tissue is built up of some fifteen to twenty duct systems. Each system consists of the main duct

opening on the surface of the nipple, of its branches, and of the acini which develop at the inner extremity of each terminal branch. The connective tissue surrounds and supports the glandular elements, the whole forming the corpus mammae which lies in the superficial fascia of the chest wall.

The breast tissue is not enclosed in a true capsule. It is not attached to the pectoral fascia on which it lies, but is attached to the overlying skin by the suspensory ligaments which, arising from the superficial fascia enclosing the breast, traverse the subcutaneous fat and are attached to the deep layers of the skin. Lymphatic vessels accompany the ligaments.

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infraclavicular triangle, to which vessels from the upper part of the breast drain.

From all these axillary lymph glands the efferent vessels pass to the supraclavicular group, which, as already indicated, may also receive vessels directly from the upper part of the breast.

2. AETIOLOGY

Age

Carcinoma of the breast is very rare under the age of 25, and increases in frequency to reach its highest incidence in the decades 40–50 and 50–60. It is thus mainly a disease of the menopause and post-menopausal period, and as the age advances the probability of a lump in the breast being cancer becomes greater.

Sex

The disease occurs very rarely in the male, accounting for less than 1 per cent of all carcinomas of the breast.

There is no definite evidence of any inherited predisposition to the disease. Striking examples of familial incidence have been recorded, but it is doubtful if it occurs with significant frequency.

It is generally accepted that there is a higher incidence in nulliparous than in parous women. It would appear to be more common in women who have borne few children than in the mothers of larger families, and in those in whom lactation has been abnormal or who have not nursed their children for the normal period. This relationship to irregular or disturbed function suggests a possible endocrine aetiological factor.

Relation to pre-existing benign lesions

The common benign tumour which occurs in the breast, the fibro-adenoma, does not tend to become malignant and cannot therefore be looked on as a dangerous or pre-cancerous lesion. The universal rule that such tumours should be removed is based on the difficulty, if not the impossibility, of differentiating clinically between a simple tumour and a small early carcinoma, rather than on the fear that the simple tumour may become malignant.

The papilloma which develops in the main ducts of the breast is not considered so innocent a lesion. There is little doubt that it may develop into a duct carcinoma, from which, indeed, it can only with difficulty be differentiated by clinical examination.

Acute mastitis

Acute puerperal mastitis is of little or no importance in the genesis of carcinoma, although very occasionally carcinoma may develop in relation to the scar of a previous incision for acute mammary abscess or to a persistent sinus following such acute infection.

Chronic cystic mastitis

The position with regard to so-called chronic mastitis is more difficult, and the problem of the relationship between this condition and carcinoma has been the subject of many investigations—histological, statistical and experimental. The epithelial hyperplasia (epitheliosis) which occurs within the ducts and cystic spaces in cystic mastitis may also be found in breasts which are the seat of carcinoma, and in such cases the appearances sometimes strongly suggest that a primary benign intraductal hyperplasia has assumed malignant characters in that it has erupted through the duct or cyst wall and invaded the surrounding tissue—that in fact it has become a carcinoma. Cheatle and Cutler (1931) state that they found conclusive evidence of the change from cystophorous desquamation to neoplasia ending in carcinoma

in about 20 per cent of all breast carcinomas. On the other hand, other investigators state that changes resembling chronic cystic mastitis are found so commonly in breasts which are considered normal that the presence of such changes along with carcinoma cannot be accepted as evidence of a causal relationship.

Again statistical studies, as, for example, of the incidence of carcinoma in patients who are known to have had chronic cystic mastitis, have at the most shown a slightly higher incidence of carcinoma in women with cystic mastitis than in the general population.

On the whole, it cannot be held as definitely proved that such atypical involutional changes as are found in this condition are of special significance in the aetiology of mammary carcinoma. From the practical point of view, we would agree with Geschickter (1943), who states that "the incidence of mammary cancer in patients with chronic cystic mastitis is too low to warrant mastectomy".

3. PATHOLOGY

Classification

Carcinoma of the breast presents such diverse forms and assumes such a variety of pathological features that a satisfactory and generally acceptable classification has not so far been found. The terms employed to describe different types of tumour, such as scirrhous, encephaloid, adeno-carcinomatous and colloid, are based on such a variety of features, clinical, cytological and degenerative, as to make classification on these lines impossible. Tod and Dawson (1937) suggest as a simple classification:

(a) Malignant growth in cystic tissue giving rise to what is clinically the larger, softer cellular type of tumour which is late in spreading to the axillary glands, and

(b) malignant growth in non-cystic tissue, characterized by early penetration of the duct wall and by spread into the surrounding tissue, often with the production of that marked fibrous tissue reaction which produces the scirrhous tumour. In this type, except in the completely involuted breast of the aged, in which the atrophic scirrhous variety is found, invasion of the lymph stream and involvement of the lymph glands is early.

Site of tumour

The commonest site for carcinoma is the upper and outer quadrant of the breast, the least common the lower and inner quadrant. The tumour may originate centrally in one of the larger ducts, in a main duct and its acini, in terminal ducts and their acini or, rarely, diffusely throughout the entire gland (Cheatle and Cutler, 1931).

Origin in ducts

Dawson (1943) suggests that all cancers of the breast are, in their initial stages, duct cancers, and that the primary tumour change, the epitheliosis, may take the form of a solid mass of cells filling up the glandular structures, of a multilayered lining of cells or of an intraduct or intracystic papillary tumour. In any case, sooner or later the duct wall is invaded, and the cells grow out to infiltrate the surrounding stroma, to invade the lymphatic vessels and to spread to the extramammary tissues.

Variations in malignancy

There are great variations in malignancy in breast cancer between the two extremes of very rapid growth and dissemination, as in carcinoma of pregnancy or lactation when the whole breast is active and the growth of the tumour is

correspondingly rapid, and very slow growth and delayed dissemination as in the aged; and there is a corresponding diversity in the microscopic appearances presented. These vary from the well-differentiated adeno-carcinoma to completely anaplastic tumours, and from densely fibrous tumours to solid masses of epithelial cells with little stroma.

Mode of spread

The tumour spreads from its site of origin first by direct extension and invasion of the gland itself, the rate and extent of the process depending upon the physiological state of the gland and on the particular type of tumour. Secondly, the tumour extends in the breast by the invasion of the peri-acinous and periductal lymphatics, secondary tumours in the gland being thus formed. Thirdly, the tumour extends beyond the limits of the breast to involve the skin on the superficial aspect, or the underlying muscles and fascia on the deep aspect. Involvement of the skin may occur (a) by direct extension, invasion and ulceration; (b) along the suspensory ligaments, the shortening of which leads to dimpling and fixation of the skin; (c) by invasion of the lymphatics of the skin blocking these vessels and producing oedema (*peau d'orange*); and (d) in a later stage, by growth up the lymph vessels to the surface, producing nodules of tumour in the skin and, when this is advanced and widespread, the condition known as cancer *en cuirasse*.

Lymphatic spread

Extension beyond the breast occurs primarily by the lymphatics, the main flow as already described being towards the axilla. From the medial part of the breast extension by lymphatics may be to the mediastinum or to the other breast and axilla, whereas from the lower and medial part malignant cells may pass in the fascial plexus in the region of the xiphoid to the peritoneum and the falciform ligament. The spread of malignant cells along the lymph vessels may be by embolism or by permeation, probably most commonly by the former.

Blood spread

Invasion of the blood stream occurs either by cells gaining access directly into the vessels at the site of the primary tumour or from lymphatic invasion through the thoracic duct. In the former case the cells may pass into the venous side of the circulation, through the right side of the heart and so reach the lungs where metastases may be produced. Batson (1940) claims to have demonstrated a blood spread by the vertebral plexus of veins which is reached by a reversal of blood flow which, he states, is occurring constantly and physiologically. Such a mechanism may well explain the common occurrence of metastases in the spine, the ribs, the skull, and so on.

Distant metastases occur as a result of dissemination of tumour cells by lymphatics or blood channels, chiefly by the latter. Although they may involve any viscus, they most commonly occur in the lungs and pleura, in the liver and in the brain. The skeletal tissues most frequently affected are the spine, the pelvis, the femur, the skull and the ribs.

4. THE CLINICAL PICTURE

Difficulties and delay in diagnosis

In discussing the clinical features and diagnosis of cancer of the breast, there is perhaps no greater necessity than to stress at the very outset the great difficulty of distinguishing a carcinoma, *in its early stages*, from other breast swellings, and the paramount importance of looking on every lump in the breast of an adult woman as a possible carcinoma, and considering it as such

until it can be proved to be something else. In many cases such proof can be obtained only by removal and microscopic examination of the tumour. Although delay in diagnosis and treatment is frequently the fault of the patient, it has been shown that the doctor and the surgeon are frequently also at fault in this matter. Two mistakes are common. (1) To ask the patient to report back for re-examination in a month or six weeks. If the condition then shows little change, the doctor's dilemma is not resolved as the condition may still be a slowly growing tumour. If sufficient change has occurred to enable a definite diagnosis of cancer to be made, valuable time has been lost. (2) An even worse course to pursue is to leave it to the patient to report back if she notices any change in the breast condition. This may be disastrous. We have known a patient report back in eighteen months.

The diagnosis of carcinoma of the breast in its early, easily curable stage is undoubtedly difficult. The diagnosis at a later stage is usually easy, the tumour presenting the classical text-book picture.

Signs in the early case

"Localized true nodularity is one of the earliest and therefore one of the most important signs of early carcinoma of the breast. It may be the only sign of early carcinoma" (Cheatle and Cutler, 1931). The nodularity is usually hard, while the rest of the breast is normal, as is the other breast. There is an absence of pain or, at least, of constant pain, and if pain occurs intermittently it is felt only at the site of the tumour. It is on these signs and symptoms, and on these only, that a diagnosis of localized carcinoma of the breast can be made.

Classical signs

Later the well-known classical signs become evident: the hard tumour more easily felt when the breast is flattened against the chest wall; dimpling of the skin over the tumour or, later, fixation of the skin to the tumour; retraction and sometimes elevation of the nipple; fixation of the tumour to the underlying fascia and muscles; absence of tenderness; the presence of enlarged axillary glands which are usually hard. There are other signs such as blood-stained discharge from the nipple, present only if the carcinoma has originated in one of the main ducts; and the signs which develop later in the disease, such as oedema of the skin, often to be found first just below the nipple, ulceration of the skin, and secondary nodules of disease in the skin.

In the much rarer diffuse form of the disease the whole of the breast may be involved. The breast tissue is hard (it feels solidified) and the breast is possibly slightly shrunken, with an irregular contour. The skin may be adherent and the nipple fixed and retracted. Pain is absent or slight and the axillary glands are involved. In the acute form of cancer the breast may feel warm to the touch, giving the impression of an inflammatory condition, and leading to the diagnosis of acute mastitis. In the same way the diffuse form of a less acute type may be looked on as a chronic mastitis.

Signs of dissemination

The clinical examination of the patient must extend beyond the breast and axilla. The supraclavicular glands and the opposite breast and axilla must be examined for secondary growths, the chest for evidence of pleural effusion (secondaries in the lungs may not cause any symptoms and not give rise to any signs on physical examination for many months), the spine for pain or tenderness, the abdomen for possible involvement of the umbilicus or the liver, and for the presence of ascites. Finally, x-ray examination, at least of the spine and pelvis and of the lungs, should be carried out in all cases in

which the apparent rapidity or the duration of the disease renders the development of distant metastases likely.

5. SPECIAL AIDS TO DIAGNOSIS

Biopsy

There is no special aid to diagnosis to compare with biopsy, which must be carried out under general anaesthesia whenever doubt exists. The tumour should be excised (not incised), the surgeon being prepared and having the patient's permission to proceed to mastectomy if by macroscopic or immediate microscopic examination of the tissue removed the diagnosis of carcinoma is confirmed. It is preferable to make a decision at once and proceed to the major operation than to do the biopsy and wait for from seven to ten days for the pathologist's report. The macroscopic features of the usual type of carcinoma which enable the surgeon to make an immediate diagnosis of malignancy from a biopsy specimen are: the tumour has no definite margin; it is hard and gritty when cut or scraped with a knife; it may show the appearance of an unripe pear on section; the cut surface tends to become concave.

Transillumination

Transillumination of the breast may give some help in diagnosis, especially in differentiating a tense cyst with clear fluid from a tumour. The former transilluminates, the latter does not. However, a cyst containing blood or turbid fluid does not transilluminate. Aspiration may be needed to confirm a diagnosis of cyst, but the possibility that carcinoma may exist in the wall of a cyst must never be forgotten.

6. DIFFERENTIAL DIAGNOSIS

(1) Chronic mastitis

This is dealt with in the section Breast—Chronic Mastitis.

(2) Traumatic lesions

(*a*) *Haematoma following injury*

The history of definite injury, the presence or history of superficial bruising, fluctuation, and aspiration of blood, will usually clear up the diagnosis. Transillumination may help.

(*b*) *Traumatic fat necrosis*

There may be no history of injury. The condition presents as a very hard lump, usually adherent to the skin which is puckered and indrawn. The signs closely resemble those of carcinoma, and biopsy is the only certain method of diagnosis. (The subject of Fat Necrosis is dealt with elsewhere in BRITISH SURGICAL PRACTICE.)

(3) Infective conditions

(*a*) *Acute mastitis*

Difficulty may arise in differentiating acute carcinoma occurring during lactation from acute puerperal mastitis, as the signs of both conditions are very similar. The general signs of an acute infection—toxaemia, fever, leucocytosis—will point to infection. The condition should be treated as such, and in a few days the diagnosis may become clear as the infective condition will show either resolution or suppuration.

(*b*) *Tuberculosis*

The disease may be present in the breast or may have extended into the breast from the chest or chest wall. In the former case differentiation from carcinoma may be almost impossible without exploration. Local reddening of the skin, local softening and sinus formation may lead to the correct diagnosis, and bacteriological confirmation may be obtained.

(*c*) *Actinomycosis*

This is extremely rare and can be definitely diagnosed only by the characteristic pus and by bacteriological examination.

(4) Benign tumours

(*a*) *Fibro-adenoma*

A smooth, firm, solid, movable, round or lobulated mass occurring in the breast of a woman under the age of 25 is almost certainly a fibro-adenoma. After this age the possibility of early carcinoma cannot be excluded without biopsy. A much larger round or lobulated tumour situated centrally may be a fibro-adenoma, and may be indistinguishable from a duct carcinoma unless fixation to the skin, a discharge of blood from the nipple, or enlarged axillary glands make the latter diagnosis fairly certain. The soft type of fibro-adenoma (the intracanalicular fibro-adenoma) may, when it reaches a large size, lead to ulceration of the overlying skin and eventually to fungation through the skin. The appearances may suggest cancer, but the relative softness of the tumour, the bloody discharge from the ulcer, the lack of invasion of the skin, and the fact that a probe can be slipped under the skin at the edge of the ulcer serve to differentiate it from a cancer which has invaded the skin. (Fig. 271.)



FIG. 271.—Large fibro-adenoma with ulceration of skin simulating carcinoma.

(*b*) *Papilloma*

Papilloma occurring in one of the ducts is the commonest cause of bleeding from the nipple, a sign which is also present, however, in some cases of duct carcinoma. The papilloma may be palpable as a soft mobile tumour, or, as it is frequently intracystic, the cyst may be palpable as such. The tumour is usually situated centrally, grows slowly and is painless, and as a rule there is no enlargement of axillary glands, and none of the other definite signs of carcinoma.

(5) Cysts

(*a*) *Single*

A single cyst may present difficulties, especially if situated deeply in the breast. The cyst is hard and tense, with a smooth, well-defined margin. Fluctuation can usually be demonstrated by fixing the cyst firmly against the chest wall with one hand and eliciting its tense, elastic character with a finger of the other hand. Transillumination is helpful and aspiration of the fluid contents

confirmatory, though blood-stained fluid from a cyst raises the question of an intracystic tumour, benign or malignant. The characteristic features of carcinoma, such as retraction of the nipple, adherence to surrounding structures and enlarged axillary glands, are absent.



FIG. 272.—Paget's disease with visible carcinoma in outer upper quadrant.

(*b*) *Multiple*

Multiplicity of swellings in itself is against a diagnosis of carcinoma, and other signs characteristic of cyst formation, though more easily demonstrated in large solitary cysts, may be elicited.

(6) Paget's disease of the nipple

(*a*) *Clinical features*

This condition presents as an ulcerative lesion of the nipple. The ulcer is superficial and may be of a brilliant red colour, or its surface may be covered by brownish scales. There may or may not be induration. There is usually a discharge from the ulcer. The nipple may project normally or it may be retracted, but it is gradually destroyed, and the lesion spreads centrifugally, retaining a more or less circular shape. (Fig. 272.)

The affected breast may show no other abnormality on clinical examination, but in a considerable proportion of cases a palpable mass, which in fact is a carcinoma, is present. Such a tumour may be situated in any part of the breast, and as a rule it is not central. (Fig. 273.)

(*b*) *Aetiology and pathology*

The precise nature of Paget's disease and the correct interpretation of the microscopic appearances have not been finally determined, but there is general agreement that it is from the outset a malignant condition. The characteristic changes in the nipple would appear to be the result of the invasion of the deeper layers of the squamous epithelium of the nipple by the malignant cells of an "intraduct cancer" (Muir, 1941) which has originated in one or more of the lactiferous ducts about the junction of these ducts with the skin of the nipple, and which spreads up and down the affected ducts by invasion or permeation of the epithelium lining the ducts. Thus the growth does not fill the duct, but grows rather as a cylinder within the duct, and it does not erupt through the wall of the duct. Similarly, when the malignant cells reach the surface epidermis they grow only in the epidermis and do not invade



FIG. 273.—Paget's disease of nipple.

the dermis. These are the typical Paget cells—large cells with clear cytoplasm and pyknotic nuclei lying among the deeper cells of the epidermis. Other characteristic microscopic appearances are the downward enlargement of the interpapillary processes of the epidermis and the round-cell infiltration of the underlying dermis. (*See* Fig. 274.)

Association with carcinoma

Paget's disease of the nipple is always associated sooner or later with a true carcinoma of the breast. The ulceration of the nipple may be present for years before the tumour becomes manifest, or the tumour may appear at an



Fig. 274.—Paget's disease of the nipple, showing the typical "Paget" cells in the epidermis. (× 150.)

early stage. Invasion of lymph glands and dissemination occur as in any breast cancer.

(c) *Diagnosis and differential diagnosis*

Any ulcerative lesion of the nipple in a woman over 40 years should raise the suspicion of Paget's disease. The ulcer may present features so typical of the condition as to make the diagnosis fairly certain: bright red colour, granular base, well-defined edges. On the other hand it may be difficult to decide whether the condition is a simple eczematous one or Paget's disease. Simple treatment, as for a benign eczema, may in a few weeks clear up the condition and the diagnosis. If the lesion fails to respond, biopsy should be carried out.

Other affections of the nipple which may give rise to doubt are simple papilloma, squamous epithelioma and rarely a primary chancre.

A careful examination of the breast for a tumour and of the axilla for enlarged lymph glands should, of course, never be omitted.

(*d*) *Treatment*

Paget's disease is treated as carcinoma of the breast, either by the radical operation or, particularly if no tumour can be found, by simple mastectomy and radiotherapy. In cases in which doubt exists it is safer to do a simple mastectomy, submit the breast for examination, and if the disease is found to be present, give post-operative radiotherapy.

7. TREATMENT

The standard treatment of carcinoma of the breast is the radical operation. The only other form of treatment which has met with any success is radiotherapy, either by radium or by x-rays, but up to the present time this form of therapy has not been developed to such an extent that it can be looked on as an accepted alternative to operation. Nevertheless radiotherapy is playing an increasing part in the treatment of breast cancer, for it is now widely used along with surgery, either pre-operatively or, more commonly, post-operatively.

(1) Indications for radical operation

The radical operation is indicated in all cases of carcinoma of the breast if the patient is judged to be fit to stand the operation and if the disease has not advanced to the stage of inoperability. With modern anaesthesia and methods of resuscitation, the vast majority of cases can be submitted with a high degree of safety to the radical operation. Operation alone must be relied on if effective radiotherapy cannot be given, that is, if the requisite apparatus and the services of a highly trained radiotherapist are not available.

(2) *Contra-indications to radical operation*

It may not be feasible to carry out the radical operation because of the general health of the patient. Great age and serious disease may be obvious contra-indications. All other contra-indications are due to the advanced state of the disease. These may be classified as follows:

(i) *Acute form of carcinoma.*—The so-called inflammatory type—carcinoma developing in pregnancy or lactation.

(ii) *Local signs of advanced disease.*—Extensive oedema of the skin over the breast; tumour nodules in the skin over the breast; intercostal or parasternal tumour nodules.

(iii) *Signs of advanced disease in lymph glands.*—Oedema of the arm; involvement of supraclavicular lymph glands.

(iv) *Evidence of distant metastases.*—For example, in bone, lungs, pleura, abdomen, and so on.

(v) *Presence of two or more of the following signs.*—Ulceration of the skin, oedema of the skin even of limited extent (less than one-third of the breast), fixation of the tumour to the chest wall, gross involvement of axillary glands, fixation of axillary glands to the skin or deep structures.

There is evidence to support the view that performance of the radical operation when the disease is locally far advanced actually shortens the patient's life. Radiotherapy, alone or combined with limited surgery, is the only form of treatment to be recommended in such cases.

(3) Indications for treatment by radiotherapy alone

It has been indicated that there are no fully valid reasons for adopting radiotherapy alone as the treatment of choice of "operable" breast cancer, because this form of treatment is not sufficiently established as an effective method to justify its general use in place of radical operation. Nevertheless there are cases in which radiotherapy should be used: (1) if the patient refuses operation; (2) if the patient is considered unfit on general grounds for operation; (3) if the radical operation is contra-indicated by extensive local spread of the disease.

Radiotherapy is given either in the form of deep x-rays or by means of radium. Keynes (1932) developed the technique of treatment by interstitial radium and demonstrated that the method could be used successfully, either alone or combined with surgery. Radium, however, has been largely superseded by x-ray therapy, which is now generally considered to be the more effective and reliable method.

(4) Indications for combined surgery and radiotherapy

X-ray therapy when used in combination with surgery may be given either before or after operation. In either case it must be given in adequate dosage, and its main limitation must be realized: it cannot affect malignant cells which have already spread beyond the area which is irradiated.

(a) *Pre-operative radiotherapy*

The purpose of pre-operative x-ray treatment is to destroy or devitalize malignant cells which may have spread from the primary tumour, for example, cells permeating lymphatic vessels, and so lessen the risk of active malignant cells being disseminated during the operation. This treatment may be designed to destroy the primary tumour or may be used to destroy superficial extensions of the tumour, such as skin nodules, and so make possible some limited form of surgery.

(b) *Post-operative radiotherapy*

At the present time post-operative irradiation is preferred to pre-operative x-ray therapy and the grounds for this preference appear to be sound. There are two ways in which post-operative x-ray treatment may be used along with surgery: (i) the radical operation followed by x-ray treatment; (ii) a limited operation followed by x-ray treatment.

(i) *Radical operation plus radiotherapy.*—Post-operative irradiation is designed to destroy any malignant cells which may have been left in the operation wound, cells which have possibly been scattered throughout the wound as a result of the operation. That such "seeding" of the wound occurs during the operation is shown by the fairly high percentage of local recurrences which appear within a year or two of operation. Post-operative radiotherapy can deal fairly effectively with this danger, but to be fully effective it must be given soon after the operation and in adequate dosage. Unfortunately this is not always possible, for the somewhat stretched and atrophic skin, adherent to the chest wall, is not in good condition to withstand the effect of the x-rays and, owing to delayed healing which not infrequently occurs after the radical operation, or to the fact that skin grafting has had to be used to close a skin defect, treatment by x-rays has to be delayed, often for a

considerable time. As a result, irradiation following the radical operation is often delayed and inadequate.

To get over these difficulties a limited operation may be performed; how limited is not yet finally determined. The objects of limiting the operation are: (1) to ensure primary healing of the skin, (2) to leave healthy, well-nourished, non-adherent skin, (3) to limit the extent of the dissection and so the area over which cells may be disseminated at the operation.

(ii) *Simple mastectomy plus radiotherapy.*—These objects may be accomplished by performing a simple mastectomy, removing the breast down to, but not including, the pectoral fascia, removing a limited amount of skin, not extending the wound downwards to the epigastrium, and not dissecting the axilla unless there are *large* lymph glands present: the radiotherapist claims to be able to deal with moderate glandular involvement. Such a scheme of treatment is still on trial, but McWhirter claims results from it which surpass those obtained by any other form of treatment. This method is not suitable for very fat patients, for those in whom the tumour is invading the pectoral muscles, or for those with fairly massive axillary involvement. In such cases the radical operation is to be preferred. On the other hand, certain fairly advanced cases may be treated on these lines with better results than have been obtained by the radical operation, probably because the dissection of the axilla in the presence of extensive glandular involvement leads to gross spilling of malignant cells locally, and to dissemination of such cells to other parts. (*See* Breast-Carcinoma of, Post-Operative Radiotherapy, p. 475.)

(5) The radical operation

An extensive area of skin is prepared for operation in the usual way. General anaesthesia is used, gas-oxygen-ether or cyclopropane. The patient lies supine on the operating table with the arm, supported on a suitable arm rest, in 90 degrees abduction.

The incision

The incision for a carcinoma situated centrally, or in the upper and outer, or lower and inner quadrant, begins in the epigastrium and passes upwards and outwards towards the anterior axillary fold. It splits to enclose the tumour and the nipple, the diverging limbs passing 2 inches wide of the corresponding edges of the tumour, so that a 2-inch margin of skin is removed all round the tumour. The two incisions meet as they approach the anterior axillary fold, and the single incision then passes 1 inch or so medial to and above this fold and terminates over the insertion of the pectoralis major muscle, or is carried backwards across the axilla from anterior to posterior wall. All these incisions should be about ½ inch deep if the thickness of the subcutaneous tissue allows of this. (Fig. 275.)

The incision may require modification for tumours situated towards the lateral or medial margin of the breast. In such cases an incision similar to the above is made enclosing the nipple, and lateral or medial extensions are made from it enclosing the tumour and the 2-inch margin of skin around it. An alternative method is to use a transverse elliptical incision with extensions towards the axilla and the epigastrium.

Skin flaps

The skin flaps are raised medially and laterally, a thin layer of subcutaneous tissue, about ¼–½ inch, being raised with the skin in order to conserve its blood supply. The undermining incisions are carried to the opposite margin

of the sternum, and, in the epigastrium, beyond the linea alba medially, to the posterior axillary fold laterally, to the clavicle above, and to the level of the sixth rib inferiorly. If, as is suggested, the axilla be dissected before the breast is removed, only the upper part of the skin flaps should be raised before proceeding with the axillary dissection.

Exposure of the axilla

The interval between the sternal and clavicular portions of pectoralis major is sought and defined, and a finger inserted into this interval picks up the acromio-thoracic vessels which are clamped and divided (Fig. 276). The two portions of the muscle are separated towards their insertion and the sternal portion is divided close to the humerus. The cut end of the muscle is retracted medially, exposing pectoralis minor and the costo-coracoid membrane (Fig. 277). The latter is divided close to the clavicle and the muscle divided at its attachment to the coracoid process and turned downwards and inwards, thus opening up the axilla (Fig. 278).

Dissection of the axilla

The removal of the axillary contents begins at the apex. After incising the fascia over the axillary vessels the fat and glands are dissected downwards by gauze dissection. The most proximal part of the axillary vein is cleared first, and as the dissection passes outwards the various tributaries entering the vein come into view. Each is doubly clamped and divided close to the main trunk (Fig. 279). The downward displacement of the axillary contents brings the subscapularis muscle with its covering fascia into view. The latter is incised as far medially as possible, and stripped laterally off the muscle till the subscapular vessels and nerves are reached. These should be preserved but stripped clear of fat and glands. At this stage the intercosto-brachial nerve will be seen crossing the axilla and has to be sacrificed. As the medial wall of the axilla is cleared, the nerve to serratus anterior is seen running vertically downwards on the chest wall and is preserved. The dissection continues downwards till the lower border of latissimus dorsi is reached, by which time the whole axillary contents should have been freed and displaced downwards and medially together with the cut ends of the two pectoral muscles. A hot pack is now placed in the axilla and removal of the breast, pectoral muscles and a wide area of fascia proceeded with. (Fig. 280.)

Removal of breast and pectoral muscles

The raising of the skin flaps is first completed, and the removal of the muscles and fascia from the chest wall is begun by incising the fascia in front of the nerve to serratus anterior. (Fig. 281.) The fascia is stripped medially and the pectoral muscle origins raised from the ribs as the dissection proceeds. The lateral branches of the intercostal vessels are seen and divided after being clamped as they are met. In the lower limit of the dissection, the fascia over the serratus and external oblique digitations is stripped off and, as the midline is approached, the fascia over the upper part of the rectus muscle is removed.

As the sternum is approached the anterior perforating branches of the internal mammary artery are found coming through the intercostal spaces. They can be seen and clamped before division. (Fig. 282.) The sternal origin of pectoralis major is removed completely, and the fascia over the sternum elevated and removed. Thus the whole mass of tissue, axillary glands and fat, breast, pectoral muscles and fascia is raised off the chest wall in one piece, working from the axilla and lateral side towards the midline. (Fig. 283.)

All vessels divided in the course of the dissection are immediately caught. Throughout the operation hot towels should be placed and replaced as

required, to cover the extensive wound and to minimize oozing and prevent cooling. All vessels are then tied or coagulated with diathermy, a careful inspection of the wound for bleeding points is carried out, and, when these have been dealt with, closure of the wound is proceeded with. The wound should always be drained, one or two rubber-dam strips being used, one

Drainage of wound

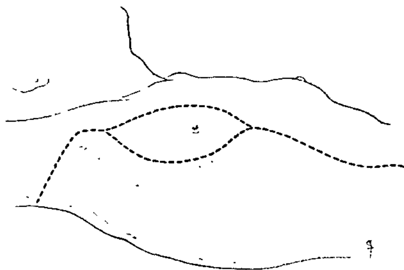


Fig. 275.—The outline of the skin incision as employed when the disease occupies a central position in the breast.

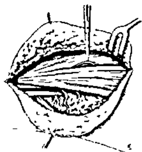


Fig. 276.—The first stage of the axillary dissection. The separation between the sternal and the clavicular fibres of the pectoralis major muscle is defined, and in the space the acromio-thoracic vessels are isolated and ligated.



Fig. 277.—The fibres of the pectoralis major muscle have been divided and the central portion is retracted. The pectoralis minor muscle is in view. The acromio-thoracic vessel is seen piercing the costo-coracoid membrane at the upper edge of the muscle.

inserted through a stab opening in the lateral skin flap, as far back as possible and a little below the axilla to drain the axilla and upper part of the wound, and the second should be placed to drain the lower part. The skin edges are then approximated by sutures and clips. It is usually possible to get complete closure of the wound without tension if undermining has been widely carried out. Complete closure is always desirable, but should not be attempted if it is

Closure of wound

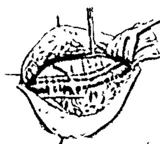


FIG. 278.—Both pectoral muscles have been divided and the central ends retracted. The axillary area is now fully exposed to view.

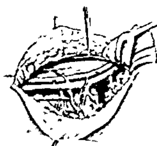


FIG. 279.—The dissection of the axilla has been carried a stage further. The main vessels are defined and cleared by gauze dissection, and various junctional vessels are ligated.



FIG. 280.—The preliminary dissection of the axilla has been completed. The various junctional vessels have been ligated with the exception of the subscapular group, the subscapular nerves are in view, and the long thoracic nerve can be seen on the lateral chest wall



FIG. 281.—The exposure of the breast has been secured by dissection of the skin edges, and the limit of division of the fascia has been outlined.

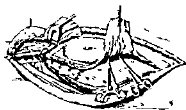


FIG. 282.—The subfascial and submuscular dissection is continued. The lateral thoracic vessels have been ligated, and the anterior perforating branches are being secured.

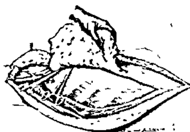


FIG. 283.—The final stage of the submuscular dissection. The various vessels have been secured, and the muscles are being severed from their sternal attachments.

likely to cause tension and consequent necrosis of skin: it is preferable that a gap should be left and the defect closed by skin grafting. If closure has been accomplished but has resulted in pallor of some areas of skin owing to tension, some relief may be obtained by making multiple superficial cuts or scratches with the knife sufficiently deep just to reach the dermis. These small incisions, $\frac{1}{2}$–$\frac{3}{4}$ inch in length, should bleed slightly if the skin is viable, and as they gape a little they undoubtedly relieve the tension and so help to maintain viability.

Post-operative care

Shock due to excessive blood loss should be treated by blood transfusion. The patient should be nursed with the arm supported in an abducted position. Drains are removed on the second or third day after operation and clips and stitches are removed at the usual time. Exercises designed to restore shoulder movements should be carried out after the wound has healed.

(6) Simple mastectomy with radiotherapy

For the technique of simple mastectomy when the operation is used in combination with radiotherapy, the reader is referred to the article on Post-Operative Radiotherapy for Carcinoma of the Breast, p. 484.

8. RESULTS OF TREATMENT

Operative mortality

The radical operation carries a definite post-operative mortality, probably in the region of from 3 to 5 per cent. In the less extensive procedures such as simple mastectomy the mortality is negligible. The causes of death are post-operative shock, pulmonary embolism, other vascular accidents, chest complications and sepsis.

Post-operative disability

There is frequently some loss of movement at the shoulder joint after the radical operation due to the scar in the axilla and to failure to carry out active exercises in the post-operative period.

Post-operative oedema of the arm occurs in a proportion of cases. It is a result of the close dissection of the axilla, of the extensive exposure of the axillary vein, and of the consequent scarring round the vein. It is to be distinguished from oedema of the arm due to recurrence of the disease in the axilla.

X-ray treatment may sometimes cause fibrosis of the muscles in the irradiated area. The muscles become hard and "frozen" and there is great limitation of shoulder movements.

Cure of the disease

It is exceedingly difficult to give accurate figures to illustrate the results of treatment. If *all* cases (operable and inoperable) admitted to a general hospital are considered, the over-all five-year survival rate is in the region of 20 per cent. The five-year survival rate for *all operable* cases treated by radical operation alone is probably about 40 per cent. The five-year survival rate is, of course, much higher if the disease is confined to the corpus mammae, with no involvement of skin or fascia, or lymph glands. The rate is reduced approximately by half if lymph glands are already involved at the time of operation.

For the same group of cases—*all operable* cases—McWhirter quotes a five-year survival rate of 55·9 per cent following treatment by simple mastectomy plus post-operative radiotherapy. (*See* article on Post-Operative Radiotherapy for Carcinoma of the Breast, p. 480.)

9. FACTORS INFLUENCING PROGNOSIS

(1) Age

It has been widely taught that the age of the patient is an important prognostic factor in carcinoma of the breast, particularly in the sense that the younger the patient the worse the prognosis. This statement is too sweeping and very probably misleading. Among the higher age groups there is surprisingly little difference; probably the prognosis is better between the ages of 45 and 65 than in women over 65.

(2) Pregnancy and lactation

There is general agreement that when the disease appears during pregnancy or lactation the prognosis is bad. So seldom is radical surgery successful in such cases, that treatment by simple mastectomy and radiotherapy, or by radiotherapy alone, is to be preferred.

(3) Duration of the disease

The duration of the disease, *per se*, is not of prognostic value. The extent to which the disease has progressed, and the type of tumour, must also be taken into consideration. Thus whereas nearly half the total number of five-year cures in one series had been treated within three months of the discovery of the disease, one-half of the remainder, that is one-quarter of the total number, had had the disease for one year or more. End results are determined, therefore, more by natural selection than by early treatment. This is, of course, no argument against early treatment, which is always desirable.

(4) Extent of the disease

This is of great prognostic significance. As long as the disease is confined to the breast tissue the prognosis is excellent and the probability of cure is high. As soon as malignant cells have left the breast as shown by involvement of regional lymph glands, the five-year survival rate falls steeply. With extensive lymph gland involvement, and still more when distant metastases are present, the ultimate prognosis is extremely poor.

(5) Type of tumour

From the prognostic point of view the tumours may be divided into two groups (*see* classification of tumours under (3) Pathology): (a) those which metastasize early, and (b) those which remain localized for long periods of time. As already indicated, the prognosis depends largely upon the type of tumour present, the tumour which metastasizes early giving a much worse prognosis than the tumour which does not.

(6) Site of tumour

Prognosis is influenced by the site of the tumour to the extent that tumours in the medial part of the breast metastasize to lymph glands within the thorax, where they are inaccessible to surgery and relatively inaccessible to radiotherapy. The prognosis in such cases is therefore worse than it is for tumours arising in other parts of the breast.

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BREAST—CARCINOMA OF, POST-OPERATIVE RADIOTHERAPY

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1. INTRODUCTION

78.] The following account of the value of radiotherapy in the treatment of breast cancer is based essentially upon the results of the investigation which is being conducted in the Royal Infirmary, Edinburgh. The investigation began in 1935, but the figures for 1930 to 1934 have been included, for they serve to some extent as a control.

Halsted operation as standard

The radical Halsted operation and its modifications have for long been accepted as the standard method of treatment of breast cancer. When any new method is introduced comparison must be made against this standard.

However, before comparison can be made it is essential to know the true value of the radical operation in the treatment of breast cancer. Surprisingly enough this figure is not easily obtainable. Published accounts vary greatly. The operation presents no great technical difficulty and the variation must be due to the degree of selection of cases. As a rule only the results of cases actually treated by (that is, selected for) the radical operation are given but the true value of the radical operation cannot be judged from these figures alone and account must also be taken of the total number of cases from which the selection was made. For obvious reasons the published figures (even when the number of "inoperable" cases is stated) of any one surgeon cannot be accepted as providing a true indication of the value of the radical operation. This value can only be assessed from the publications of large general hospitals in which the survival rates are expressed as percentages of the *total cases* referred to the hospital.

Standard of operability

When the results of the "operable" and "inoperable" cases are given separately the standard of operability must be stated. Throughout this paper the following standard of operability has been accepted.

The primary tumour, which may be of any size, may show any degree of skin involvement up to and including ulceration, but there must be no isolated skin nodules, and no invasion of the cutaneous lymphatics.

The tumour may be fixed to the pectoral muscle but must not be fixed to the ribs.

The axillary glands of the same side may be enlarged but they must not be fixed.

The supraclavicular glands must not be enlarged and there must be no clinical or radiographic evidence of more distant metastases.

In recent years there is good reason to believe that almost all the cases of carcinoma of the breast in the south-east of Scotland have been referred to the Royal Infirmary, Edinburgh, and examination of 1,334 cases referred during the period 1941–45 shows that 70 per cent can be classed as "operable" and 30 per cent as "inoperable". When the results obtained from the radical operation are applied to these figures a 5-year survival rate of 37 per cent is obtained in the "operable" group. This is in fair agreement with many of the published accounts. None of the "inoperable" cases, treated by radical operation alone, survived 5 years. When all the cases ("operable" and "inoperable") are included a 5-year survival rate of 25 per cent is obtained.

Defects of radical operation

From the above figures it will be seen that even when cases are suitable for operation 63 per cent die of cancer before the end of the 5 years and that 30 per cent are too advanced for the radical operation when they are first seen. The radical operation, therefore, fails in a high proportion of cases and there is good reason for exploring other methods of treatment. The possibility of improving the results in the "operable" group of cases will first be considered.

2. OPERABLE CARCINOMA OF THE BREAST

There are essentially two reasons why the radical operation should fail in "operable" cases.

(1) Malignant cells may be left behind locally in the chest wall and axilla, and/or,

(2) Malignant cells may have escaped beyond the area of the operation before this was undertaken.

For the present we are concerned primarily with the first cause of failure.

Residual malignant cells producing local recurrence

It is, of course, impossible to tell just how frequently malignant cells are left behind locally, but some indication of this may be gained by noting the frequency of local recurrences which appear at a later date. So that

TABLE I

THE LOCAL RECURRENCE RATE IN 364 "OPERABLE" CASES TREATED BY RADICAL SURGERY ALONE

YEARS AFTER TREATMENT	NUMBER OF LOCAL RECURRENCES	NUMBER EXPOSED TO RISK	CHANCE OF DEVELOPING LOCAL RECURRENCE IN ANY ONE YEAR	NUMBER DEVELOPING LOCAL RECURRENCES TOTAL = 100
1	69	341·5	0 202	20 2
2	20	232·5	0 086	6 9
3	16	183·5	0 087	6·4
4	8	148	0 054	3·6
5	3	119	0 025	1·6

comparison may be made with cases treated by post-operative radiotherapy, the supraclavicular region has been included in the area in which the recurrences are regarded as local.

It is doubtful if the frequency of local recurrences after the radical operation is fully appreciated. Table I shows that the number developing local recurrences within 5 years is almost 40 per cent of the total. These local recurrences will sooner or later give rise to distant metastases and cause the death of the patient but if they could have been prevented the patient's life might have been saved (provided distant metastases were not present as well). *Significance of local recurrence*

It was decided to find out to what extent local recurrence could be prevented by post-operative x-ray therapy to the chest wall, axilla and supraclavicular region of the side affected. The results in 278 "operable" cases so treated were as follows: *Prevention by post-operative x-ray therapy*

TABLE II

THE LOCAL RECURRENCE RATE IN 278 "OPERABLE" CASES TREATED BY RADICAL SURGERY AND POST-OPERATIVE RADIOTHERAPY

YEARS AFTER TREATMENT	NUMBER OF LOCAL RECURRENCES	NUMBER EXPOSED TO RISK	CHANCE OF DEVELOPING LOCAL RECURRENCE IN ANY ONE YEAR	NUMBER DEVELOPING LOCAL RECURRENCES TOTAL = 100
1	9	271	0 033	3·3
2	13	220 5	0 059	5·7
3	5	171·5	0 029	2·7
4	2	129·5	0 015	1·4
5	1	86	0 012	1·0

The number developing local recurrences within 5 years is reduced to 14 per cent of the total.

By reducing the number of local recurrences which might be expected the survival rate should be improved and the following tables show that this is so.

TABLE III

SURVIVAL RATE OF 390 "OPERABLE" CASES TREATED BY RADICAL SURGERY ALONE

YEARS AFTER TREATMENT	NUMBER OF CANCER DEATHS	NUMBER EXPOSED TO RISK	CHANCE OF DYING IN ANY ONE YEAR	SURVIVAL RATE (PERCENTAGE)
1	87	390	0 223	77·7
2	73	301	0·243	59 0
3	35	225·5	0 156	49 8
4	24	187	0 128	43 4
5	22	157·5	0 140	37·3

The difference in the results is statistically significant and the figures demonstrate clearly that post-operative radiotherapy by destroying the cells left behind in the operation area can improve the survival rate.

TABLE IV

SURVIVAL RATE OF 308 "OPERABLE" CASES TREATED BY RADICAL SURGERY AND POST-OPERATIVE RADIOTHERAPY

YEARS AFTER TREATMENT	NUMBER OF CANCER DEATHS	NUMBER EXPOSED TO RISK	CHANCE OF DYING IN ANY ONE YEAR	SURVIVAL RATE (PERCENTAGE)
1	35	307	0·114	88 6
2	49	260	0 188	71·9
3	25	195·5	0·128	62·7
4	17	162	0·105	56·1
5	9	125	0 072	52·1

Limited effect of x-ray therapy

It must be noted, however, that a successful result will not be obtained if cells have escaped beyond the area to be treated by x-rays, for cells escaping to distant sites are not influenced in any way by the localized radiotherapeutic treatment. Some cells may have escaped to distant sites before the operation was performed but the possibility of cells escaping beyond the operation area, either at the time of operation or at least before x-ray treatment could be applied, must now be considered.

Risk of dissemination of cells by operation

The trauma of the operation and the opening up of tissue planes, especially in the axilla where an "*en bloc*" dissection is difficult to perform and where many lymphatic trunks must be cut across, strongly suggest that dissemination of cells may take place before x-ray therapy can be applied. In an attempt to overcome this difficulty it was decided to explore the possibilities of treatment by simple mastectomy followed by post-operative radiotherapy.

It is true that cells may still be liberated when a simple mastectomy is performed, but in view of the fact that the axillary drainage system is not interfered with, it is unlikely that the cells so liberated will pass beyond this barrier.

Case for simple mastectomy

By not dissecting the axilla the risk of dissemination of cells from the axilla at the time of operation is eliminated.

The average interval between the operation and x-ray therapy is less than with the radical operation, for there is rarely any delay in healing after a simple mastectomy has been performed. The interval during which cells may escape to distant sites is thus reduced.

The operative mortality (accepted as the percentage of deaths, from any cause whatever, occurring within 1 month of the time of the operation) is less than that with the radical operation.

It may be maintained that the treatment of the axillary glands by radiotherapy alone is a disadvantage. In reply it may be stated that if the axillary glands are not secondarily involved the operation is unnecessary and that when the axillary glands are involved the results from operation are poor. It remains to be seen whether radiotherapy will prove more effective than operation in the treatment of the axilla.

The whole question of introducing the above method of treatment was fully discussed at a meeting of the Surgical Staff of Edinburgh Royal Infirmary early in 1941. From the apparently good results obtained in the few cases actually treated by this method before 1941 it was decided to adopt it for a period during which the results would be closely examined.

The results already published by Keynes (1928) further support the adoption of this method. It will be recalled that Keynes advised radium implantation following the local removal of the primary tumour or simple mastectomy if the tumour was large. He strongly advised against dissection of the axilla. *Radium implantation after simple operation*

Once the method was introduced it soon became obvious that it was possible to apply this method of treatment to almost every case, and certainly it could be applied to far more cases than was possible when the radical operation preceded x-ray therapy. As already mentioned, delay between the radical operation and the application of radiotherapy was often considerable, and in some cases the tumour had already recurred so extensively that only palliative radiotherapy could be given. Sloughing of the skin margins in a few cases so delayed the application of x-ray therapy that this became of doubtful value. In other cases the skin was so adherent to the ribs and so atrophic after the radical operation that either radiotherapy was not possible or the dosage had to be so reduced that it served little useful purpose. Because of the wider applicability of simple mastectomy and radiotherapy it is instructive to consider the results of treatment in all the "operable" cases in the three main periods under review.

In the period 1930–34 the main method of treatment was radical surgery alone.

In the period 1935–40 the main method of treatment was radical surgery followed by radiotherapy but for reasons already given the method could not be applied to all cases. (It must also be mentioned that in the earlier part of this period not all the cases were referred for radiotherapy.)

In the period 1941–45 almost all the cases were treated by simple mastectomy and post-operative radiotherapy.

Post-operative deaths have not been excluded from any of the Tables. Indeed it has been assumed that the post-operative mortality in cases operated on outside the Royal Infirmary was the same as that within the Infirmary, and the deaths assumed to have taken place have been entered in the tables.

The following Tables show the results obtained in all the "operable" cases in each period and, while the main method of treatment was as indicated, cases not so treated are included.

TABLE V

THE SURVIVAL RATE OF ALL "OPERABLE" CASES IN THE PERIOD 1930–34

Main Method of Treatment—Radical Surgery Alone
Total Cases = 359

YEARS AFTER TREATMENT	NUMBER OF CANCER DEATHS	NUMBER EXPOSED TO RISK	CHANCE OF DYING IN ANY ONE YEAR	SURVIVAL RATE (PERCENTAGE)
1	89	358	0·249	75·1
2	66	267·5	0·247	56·6
3	32	200·5	0·160	47·5
4	19	166	0·114	42·1
5	22	142	0·155	35·6

TABLE IV

SURVIVAL RATE OF 308 "OPERABLE" CASES TREATED BY RADICAL SURGERY AND POST-OPERATIVE RADIOTHERAPY

YEARS AFTER TREATMENT	NUMBER OF CANCER DEATHS	NUMBER EXPOSED TO RISK	CHANCE OF DYING IN ANY ONE YEAR	SURVIVAL RATE (PERCENTAGE)
1	35	307	0·114	88·6
2	49	260	0·188	71·9
3	25	195·5	0·128	62·7
4	17	162	0·105	56·1
5	9	125	0 072	52·1

Limited effect of x-ray therapy

It must be noted, however, that a successful result will not be obtained if cells have escaped beyond the area to be treated by x-rays, for cells escaping to distant sites are not influenced in any way by the localized radiotherapeutic treatment. Some cells may have escaped to distant sites before the operation was performed but the possibility of cells escaping beyond the operation area, either at the time of operation or at least before x-ray treatment could be applied, must now be considered.

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The trauma of the operation and the opening up of tissue planes, especially in the axilla where an "*en bloc*" dissection is difficult to perform and where many lymphatic trunks must be cut across, strongly suggest that dissemination of cells may take place before x-ray therapy can be applied. In an attempt to overcome this difficulty it was decided to explore the possibilities of treatment by simple mastectomy followed by post-operative radiotherapy.

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The operative mortality (accepted as the percentage of deaths, from any cause whatever, occurring within 1 month of the time of the operation) is less than that with the radical operation.

It may be maintained that the treatment of the axillary glands by radiotherapy alone is a disadvantage. In reply it may be stated that if the axillary glands are not secondarily involved the operation is unnecessary and that when the axillary glands are involved the results from operation are poor. It remains to be seen whether radiotherapy will prove more effective than operation in the treatment of the axilla.

The whole question of introducing the above method of treatment was fully discussed at a meeting of the Surgical Staff of Edinburgh Royal Infirmary early in 1941. From the apparently good results obtained in the few cases actually treated by this method before 1941 it was decided to adopt it for a period during which the results would be closely examined.

In many of these cases with extensive but localized involvement it will be generally agreed that the radical operation is an unsuitable method of treatment. Simple mastectomy, however, has a wider application and, as the investigation is concerned with the true value of any procedure and not merely with the results obtained from treated cases, it is necessary again to consider the results in all the "inoperable" cases, however treated, in each of the three main periods.

In the period 1930-34 few cases were recorded and as indicated earlier none survived for 5 years.

TABLE VIII

THE SURVIVAL RATE OF ALL "INOPERABLE" CASES IN THE PERIOD 1930–34

Main Method of Treatment—Radical Surgery Alone
Total Cases = 33

YEARS AFTER TREATMENT	NUMBER OF CANCER DEATHS	NUMBER EXPOSED TO RISK	CHANCE OF DYING IN ANY ONE YEAR	SURVIVAL RATE (PERCENTAGE)
1	22	33	0·667	33·3
2	6	10·5	0·571	14·3
3	3	4	0·750	3·6
4	1	1	1·000	0·0
5	0	0	—	0·0

In the period 1935–40 the number of "inoperable" cases referred was 221, and at the end of 5 years only 2·5 per cent were alive. Though this group was given x-ray treatment, the results are little different from those obtained from radical surgery alone and suggest that the post-operative radiotherapy was rendered ineffective by the dissemination of cells at the time of the operation.

TABLE IX

THE SURVIVAL RATE OF ALL "INOPERABLE" CASES IN THE PERIOD 1935–40

Main Method of Treatment—Radical Surgery and Post-operative Radiotherapy
Total Cases = 221

YEARS AFTER TREATMENT	NUMBER OF CANCER DEATHS	NUMBER EXPOSED TO RISK	CHANCE OF DYING IN ANY ONE YEAR	SURVIVAL RATE (PERCENTAGE)
1	137	221	0·620	38·0
2	55	84	0·655	13·1
3	13	29	0·448	7·2
4	9	15·5	0·581	3·0
5	1	6	0·167	2·5

In the period 1941–45 the number of "inoperable" cases was 404. (Table X.) Again the results are higher than any obtained before, and the difference is statistically significant when comparison is made with either of the two preceding periods. When only the localized "inoperable" cases are considered the five-year survival rate is 24·6 per cent. This figure perhaps shows still more clearly the advantages of the method of treatment advocated, for when

TABLE VI

THE SURVIVAL RATE OF ALL "OPERABLE" CASES IN THE PERIOD 1935–40

Main Method of Treatment—Radical Surgery and Post-operative Radiotherapy
Total Cases = 569

YEARS AFTER TREATMENT	NUMBER OF CANCER DEATHS	NUMBER EXPOSED TO RISK	CHANCE OF DYING IN ANY ONE YEAR	SURVIVAL RATE (PERCENTAGE)
1	94	568·5	0·165	83 5
2	102	472·5	0·216	65·5
3	52	366	0·142	56·2
4	42	307 5	0·137	48·5
5	24	261	0 092	44·0

TABLE VII

THE SURVIVAL RATE OF ALL "OPERABLE CASES IN THE PERIOD 1941–45

Main Method of Treatment—Simple Mastectomy and Post-operative Radiotherapy
Total Cases = 941

YEARS AFTER TREATMENT	NUMBER OF CANCER DEATHS	NUMBER EXPOSED TO RISK	CHANCE OF DYING IN ANY ONE YEAR	SURVIVAL RATE (PERCENTAGE)
1	75	941	0 080	92 0
2	76	668·5	0·114	81·6
3	57	440	0·130	71·0
4	31	230·5	0·135	61·5
5	8	88	0 091	55·9

The survival rates for the period 1941–45 are higher than in any of the preceding periods. Statistical examination shows that the differences are significant. The findings therefore suggest that by not dissecting the axilla the risk of dissemination of cells to distant sites is reduced.

This conclusion is supported by the results obtained in the "inoperable" cases.

3. "INOPERABLE" CARCINOMA OF THE BREAST

It is doubtful if surgeons fully appreciate the frequency of "inoperable" cases. Many such cases are admitted to the medical side of the hospital with jaundice, pleural effusions, paraplegia and so on, and some are never referred to hospital at all unless their reference is specially requested.

Localized inoperable disease

It was not, of course, possible (or advisable) to treat all cases by the method adopted for each period, for many cases were too advanced for any form of treatment or required only palliative treatment. The survival rate as a whole, therefore, will be influenced by the effect produced on those cases in which the disease is still to some extent localized, i.e. in patients with fixed axillary glands, supraclavicular involvement or involvement of the cutaneous lymphatics over the breast but with no evidence of more distant spread. In 205, or 51 per cent of the "inoperable" cases seen during the period 1941–45 the disease was apparently still localized, whereas in the remaining 199, or 49 per cent of the total, there was clear clinical or radiographic evidence of distant metastases.

TABLE XII

THE SURVIVAL RATE OF ALL "OPERABLE" AND "INOPERABLE" CASES REFERRED IN THE PERIOD 1941–45

Main Method of Treatment—Simple Mastectomy and Post-operative Radiotherapy
Total Cases = 1,345

YEARS AFTER TREATMENT	NUMBER OF CANCER DEATHS	NUMBER EXPOSED TO RISK	CHANCE OF DYING IN ANY ONE YEAR	SURVIVAL RATE (PERCENTAGE)
1	261	1,345	0·194	80 6
2	159	850·5	0·187	65·5
3	82	509·5	0·161	55·0
4	35	256·5	0·136	47·5
5	9	97	0·093	43·1

TABLE XIII

THE SURVIVAL RATE OF ALL "OPERABLE AND ALL LOCALIZED "INOPERABLE" CASES IN THE PERIOD 1941–45

Main Method of Treatment—Simple Mastectomy and Post-operative Radiotherapy
Total Cases = 1,146

YEARS AFTER TREATMENT	NUMBER OF CANCER DEATHS	NUMBER EXPOSED TO RISK	CHANCE OF DYING IN ANY ONE YEAR	SURVIVAL RATE (PERCENTAGE)
1	139	1,146	0.121	87·9
2	119	784·5	0·152	74·5
3	75	489·5	0·153	63·1
4	33	249·5	0·132	54·8
5	8	94	0·085	50·1

of deaths were actually added to the tables so as to allow for any possible post-operative deaths in cases where the operation was performed outside the Infirmary.

The findings presented suggest that the arguments advanced in favour of simple mastectomy are valid but it must be noted that however effective this method may be, it will still not affect cells which had already spread to distant sites before the patient sought treatment. It might, therefore, be of interest to give a brief account of the attempt now being made to influence these distant metastases.

5. OVARIAN IRRADIATION

By the time advice is sought the number of patients with distant metastases—whether clinically obvious or not—is high. Irradiation of the whole body is impossible for this would kill the patient long before all the malignant cells could be destroyed. From observations made, however, it would appear possible that the rate of growth of cells in distant sites may be modified by other means.

Since 1937 some patients who had distant metastases were treated by ovarian irradiation and in several a beneficial effect was obtained. It was noted that

TABLE X

THE SURVIVAL RATE OF ALL "INOPERABLE" CASES IN THE PERIOD 1941–45

Main Method of Treatment—Simple Mastectomy and Post-operative Radiotherapy
Total Cases = 404

YEARS AFTER TREATMENT	NUMBER OF CANCER DEATHS	NUMBER EXPOSED TO RISK	CHANCE OF DYING IN ANY ONE YEAR	SURVIVAL RATE (PERCENTAGE)
1	186	404	0·460	54 0
2	83	182	0·456	29·4
3	25	69 5	0·360	18 8
4	4	26	0·154	15·9
5	1	9	0·111	14·1

(as is shown in Table VIII) radical surgery was the only method of treatment available, none of these cases survived for five years.

4. SUMMARY OF "OPERABLE" AND "INOPERABLE" CASES

The analysis would not be complete without consideration of the results of all the cases—"operable" and "inoperable"—taken together. Unfortunately during the period 1930–34 no records were kept either of the patients admitted to the medical wards or of the patients who were never admitted at all. Accordingly comparison can only be made between the two periods 1935–40 and 1941–45.

TABLE XI

THE SURVIVAL RATE OF ALL "OPERABLE" AND "INOPERABLE" CASES IN THE PERIOD 1935–40

Main Method of Treatment—Radical Surgery and Post-operative Radiotherapy
Total Cases = 790

YEARS AFTER TREATMENT	NUMBER OF CANCER DEATHS	NUMBER EXPOSED TO RISK	CHANCE OF DYING IN ANY ONE YEAR	SURVIVAL RATE (PERCENTAGE)
1	231	789·5	0·293	70·7
2	157	556·5	0·282	50 8
3	65	395	0·165	42·4
4	51	323	0·158	35·7
5	25	267	0 094	32·4

The difference again is statistically significant and this in spite of the fact that the percentage of "inoperable" cases was higher in the period 1941–45 than in the period 1935–40—28 per cent against 24 per cent.

When cases with clinical or radiographic evidence of distant metastases are excluded from Table XII, the five-year survival rate rises to 50·1 per cent.

This figure is all the more remarkable when it is borne in mind that not all of the cases in Table XIII were treated by simple mastectomy and radiotherapy. Some were too elderly, whereas others suffering from advanced cardiac disease, pulmonary tuberculosis, advanced rheumatoid arthritis and so on, were quite unsuitable for treatment. It will be recalled too that a number

If there are no palpable axillary glands no dissection of this region should be performed. Superficial mobile glands in the subpectoral region and mobile glandular masses superficially placed in the base of the axilla should be removed but no attempt should be made to dissect the axilla beyond this point even though more deeply placed glands are found. If any further dissection is attempted this will defeat the whole purpose of the operation and it must be pointed out again that, if an axilla is massively involved, surgical removal of the glands will almost certainly fail to get rid of the disease and the dissection may lead to dissemination of cells beyond the area to be irradiated.

Limited dissection of axilla

If a patient is very stout it is better to perform a radical operation because in stout patients it is difficult to deliver an adequate dose to the axilla.

Supraclavicular glands should never be removed because these glands are easily and very effectively dealt with by radiotherapy and any dissection in this region may be very liable to cause distant dissemination of cells.

Radiotherapy for supraclavicular glands

It is impossible here to give a full account of the treatment by radiotherapy but the following points are important.

Only one full course of x-ray treatment should be given. The common practice of repeated courses of treatment at intervals of 3 to 6 months has never been employed. Such a practice is to be condemned and finds no place in the treatment of any form of malignant disease in which cure is to be attempted. Any treatment method so planned as to leave behind malignant cells for further treatment (and this must be so for otherwise there would be no point in subsequent courses of treatment) is just as illogical as partial surgical removal of a tumour at intervals of 3 to 6 months.

In the treatment of the axillary and supraclavicular glands it is assumed that these apparently separate groups are in fact one continuous chain of glands. Such a view seems reasonable, for at a radical operation it can be demonstrated easily that the apex of the axilla lies just deep to the medial portion of the supraclavicular region. In order to irradiate effectively this chain of potentially involved glands, two opposed fields—one anterior and one posterior—must be used. A field directed in from the base of the axilla is quite ineffective, for the fall off in dosage results in inadequate irradiation of the apex of the axilla.

In the irradiation of the chest wall tangential or glancing fields, as advocated by Finzi (1927), should be used in order to avoid lung fibrosis. Again two directly opposed fields, each 15 × 10 centimetres are used, and these fields must be so placed that no gap is left between them and the fields used to irradiate the axilla and the supraclavicular region.

Multiple field technique

Every field is treated every day over a period of 3 weeks and the minimal tumour dose delivered is 3,750r.

X-ray dosage

Because the beams must pass through bone, and in order to obtain an adequate depth-dose, a penetrating beam must be used. The beam used in this investigation is generated by a 250-kilovolt apparatus, and heavily filtered (a triple Thoraeus filter for the shoulder fields and a single Thoraeus filter for the chest-wall fields). Lower-powered apparatus with less penetrating radiation is unsuitable and when only this type of apparatus is available a radical operation should be performed.

Effects upon metastases and general health

skin nodules and glands might diminish in size, that the pains of bone metastases might become less severe or even disappear altogether and that the patients' general health might be greatly improved. These beneficial effects were not obtained in all cases but were obtained in a sufficient number to suggest that ovarian irradiation might with advantage be given routinely at the time of irradiation of the operation area.

Surprisingly enough it was found that good results could be obtained in patients after the menopause as well as in younger patients.

No originality is claimed for the above procedure, for it will be recalled that Beatson as long ago as 1896 advocated bilateral oöphorectomy in the treatment of breast carcinoma, and other workers have recorded improvement following irradiation of the ovaries.

It is too soon yet to analyse the effect on the results, and all that can be said is that the method holds out some promise of slowing down the rate of growth of any malignant cells which escape the effect of direct irradiation. The effect on the survival rate will depend upon the permanence of the effect produced. Unfortunately, there is already evidence that the malignant cells may after a time start to grow again even in cases in which the immediate effect was good.

6. TECHNIQUE OF SIMPLE MASTECTOMY AND POST-OPERATIVE RADIOTHERAPY

Effective radiotherapy essential

In a few years the evidence presented in favour of treatment of carcinoma of the breast by simple mastectomy and post-operative radiotherapy will become still more reliable, for over a thousand cases have now been treated by this method. Before this method is more generally adopted, however, it must be emphasized that simple mastectomy and a low standard of radiotherapy will be associated with results poorer than those obtained by radical operation without any radiotherapy at all.

The method of treatment is a combination of two procedures which must be adapted to each other if the best result is to be obtained.

Iodine should not be used in the pre-operative preparation of the skin, for this lowers the tolerance of the skin to radiotherapy.

Skin grafting contra-indicated

The skin incision should be of limited length so that the tissues beyond the area to be irradiated will not be contaminated with malignant cells liberated during the operation. Excess of skin should not be removed, for tension on the skin flaps is commonly associated with failure of the wound to heal by first intention and there is delay in application of radiotherapy. When the skin is involved, wide excision without radiotherapy almost always fails to get rid of the disease, and if the atrophy of the stretched skin flaps is too great it is impossible to give a full course of radiotherapy. Skin grafting does not overcome the difficulty, for grafts do not tolerate x-ray treatment well. It is an interesting observation that no patient treated by wide excision and skin grafting survived 5 years.

When the primary tumour is still mobile on the pectoral fascia the fascia should not be removed, as this leads to fibrosis of the muscle and to limitation of movement of the arm. If the tumour is firmly fixed to the pectoral fascia it is better to perform a radical operation.

BREAST—CHRONIC MASTITIS

By H. BURROWS, C.B.E., Ph.D., F.R.C.S.

1. DEFINITION AND AETIOLOGY

(*Synonyms.*—Mammary dysplasia; hormonal mastopathy; cystic mastitis; cystophorous desquamative epithelial hyperplasia of the breast.)

79.] The term "chronic mastitis" covers certain abnormal conditions of the breast, all of which appear to have the same cause, and with rare exceptions are confined to the reproductive period of life. These conditions are not inflam-



Fig. 284.—Breast tissue from a man aged 63 years before treatment with stilboestrol for cancer of the prostate.

Fig. 285.—Same man's breast after the daily administration of 17 milligrams of stilboestrol for 120 days.

matory, and therefore the term "mastitis" is inappropriate; it originated before the aetiology was known and has been retained by the inertia of custom. Experiments on animals and clinical observations on man have shown that the lesions of chronic mastitis can be induced, in the male as well as in the female (Figs. 284 and 285), by the persistent administration of oestrogen; and an excessive supply of this ovarian hormone, or an excessive response to its influence, can now, it seems, be accepted as the cause of the disease. To this statement must be added the proviso that biological phenomena which

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[References to other titles are given under Breast—Carcinoma of, Post-operative Radiotherapy in the Index Volume. The subject of Carcinoma of the Breast is also dealt with under the heading of Breast Diseases in the *British Encyclopaedia of Medical Practice* (1936), Vol. 2, p. 657.]

and is replaced by that of progesterone. The chief effect of progesterone on the mamma, after its preparation by oestrogen, is the development of glandular acini at the ends of the branching ducts. A periductal and peri-acinous oedema accompanies this process which culminates in some secretory activity in the epithelium of the ducts and acini. The action of oestrogen followed by progesterone is thus seen to be a general preparation of the mamma for lactation.

Formation of progesterone

As long as progesterone is being secreted by the ovary the pituitary is prevented from forming effective amounts of follicle-ripening gonadotrophin; the output of oestrogen from the ovary is thus for a while suspended. Only after the corpus luteum has degenerated and ceased to elaborate progesterone—the lack of which causes menstruation—does the pituitary once again supply the follicle-ripening gonadotrophin which stimulates the ovary to secrete oestrogen.

Effects of oestrogen and of progesterone

The effects of oestrogen and progesterone upon the mamma are mostly transient, and when these hormones are no longer available the breast begins to revert to its former vestigial state. During this involution the acini, and to a lesser extent the extremities of the ducts, lose their basement membrane; their epithelial cells become atrophied and dispersed, and gradually vanish. Apart from the disappearance of periductal and peri-acinous oedema the mammary stroma does not show so complete an involutionary reversion as do the epithelial structures; fibrous tissue tends to accumulate in the breast as age advances, and the adipose tissue becomes less. Doubtless the resemblance of this fibrous tissue, when excessive, to scar tissue misled clinicians of an earlier day to attribute the lesions of chronic mastitis to inflammation.



FIG. 288.—From same source as Fig. 287. Shows (above) a dilated duct occupied by a mass of swollen, globular, desquamated epithelial cells, and (below) a dilated duct with papilliferous hyperplasia (× 50).

The hormonal reactions of the breast are often specially pronounced at adolescence. To such a vigorous development of the mamma Cheatle and Cutler (1931) have applied the term "mazoplasia" (mastoplasia), which may be defined as a strong physiological response to oestrogen. The condition is to be distinguished from chronic mastitis, to which, however, it may perhaps be a forerunner.

3. MORBID ANATOMY

The mammary responses to oestrogen are not evenly distributed, nor are they invariably of a single pattern (Figs. 287, 288 and 289), and so biopsy material taken from one part of a breast may differ considerably from that taken from another part.

appear to indicate an excess of oestrogen may in some instances depend rather upon a deficiency of androgen or progestin. The interplay of these two hormones is complex, and the supply of one cannot be calculated on the basis of physiological reactions without considering the supply of the others.



FIG. 286.—Biopsy material from a man aged 54 years with gynaecomastia. Mammary epithelium is hyperplastic and is strongly basophilic. The growing duct is surrounded by fibrous tissue which is replacing the fat. The stroma next to the duct is slightly oedematous (× 50).

2. ANATOMY AND PHYSIOLOGY

Each breast consists of about 15 lactiferous ducts opening at the nipple from which they radiate in all directions through the neighbouring subcutaneous tissue. Each duct has numerous branches, at the ends of which milk-secreting acini develop.

Until puberty the breast is a small vestigial structure consisting of short and narrow ducts without acini; but from then till the menopause the ovaries secrete oestrogen and progesterone into the blood stream alternately, and these two hormones, by causing the pituitary to form mammatrophins, arouse the gland into growth and activity.

Formation of oestrogen

The normal sequence of events in each menstrual cycle appears to be as follows: the anterior lobe of the pituitary gland secretes a follicle-ripening hormone (gonadotrophin) which causes maturation of an ovarian follicle and the formation of oestrogen. The immediate effects of oestrogen on the breast are hyperaemia and slight oedema followed by growth of the ducts, hyperplasia of the *duct epithelium*, and the formation of sufficient periductal connective tissue to support the extended ducts (Figs. 286 and 287). These effects continue until ovulation occurs, whereupon the ripe ovarian follicle, its contained ovum having escaped, becomes changed into a corpus luteum; when this happens the production of oestrogen by the ovary gradually declines



FIG. 287.—Biopsy material from a woman aged 52 years with chronic mastitis. Shows dilatation of duct with hyperplasia of epithelium. The duct is surrounded by a thick layer of fibrous tissue (× 50).

mastectomy; but, whatever its degree, the pain is characterized by a variation in intensity at different stages of the menstrual cycle; it increases during the second half until a maximum is reached a few days before menstruation, at the onset of which, or shortly before, it rapidly declines. The pain is accompanied by tenderness which varies in degree in the same manner. It seems probable that the pain and tension may be attributed to the hyperaemia, oedema and secretory activity caused by progesterone in a breast already under the influence of oestrogen and affected with chronic mastitis. *Pain*

The swellings of chronic mastitis do not form hard, discrete lumps with recognizable outlines; under suitable lighting conditions they may be easier to see than to feel. Indeed, a swelling which can be clearly felt when the mamma is pressed against the chest wall by the flat of the fingers is almost certainly not attributable to chronic mastitis. When palpating a breast in this way a slightly raised surface temperature may be appreciated in the affected area; such increased warmth probably is due, in part at least, to the replacement of adipose tissue by fibrous tissue, which, as mentioned earlier, is a feature of chronic mastitis. When underlaid by a healthy layer of fat, as in the normal breast, the skin tends to be noticeably cool. *Swellings*

The increased amount of fibrous tissue and the smaller kinds of cysts can be recognized by compressing the mamma between the fingers and thumb. By sliding the palmar surfaces of the fingers gently over the front surface of the mamma the cysts can be felt, giving a sensation of small shot imbedded in the tissues; the fibrous tissue can be recognized by its tough but not hard consistence.

5. SPECIAL AIDS TO DIAGNOSIS

Transillumination by a suitable lamp may assist diagnosis. Fat, cysts filled with clear fluid, and normal breast tissue, except perhaps in the region immediately under the nipple, are translucent; tumours and blood-filled cysts are opaque; and areas of chronic mastitis, because of the increased fibrous tissue in their composition, have an intermediate degree of opacity. A palpable swelling giving a well-defined shadow suggests the presence of a tumour or an opaque cyst, whereas an intermediate degree of opacity without any distinct boundary or palpable swelling favours a diagnosis of chronic mastitis.

In some doubtful cases needling will enable the presence or absence of a cyst to be proved; moreover, the contents of a cyst may give useful information, for the presence of blood will indicate the existence of an intracystic papilloma or cancer. *Needling*

6. DIFFERENTIAL DIAGNOSIS

The chief task in diagnosis is to distinguish chronic mastitis from cancer, and this may be difficult because (1) both chronic mastitis and cancer not rarely coexist in the same breast, and (2) in its early stage cancer provides the clinician with few, if any, quite dependable and recognizable guides to its presence. Some of the main features which may be useful in distinguishing the two conditions are given in the Table overleaf.

As cancer and chronic mastitis not infrequently coexist in the same breast, the discovery of cysts or other evidence of chronic mastitis does not exclude

The leading changes of chronic mastitis are (1) hyperplasia and desquamation of the duct-epithelium, (2) enlargement and tortuosity of the ducts with dilatation of their lumina, (3) cysts, (4) an excess of stromal fibrous tissue. Leucocytic invasion may be seen, but it is normally associated with involution and therefore can hardly be included as an essential component of chronic mastitis. Intraductal and intracystic papillomas and cancer are late occurrences; whether chronic mastitis plays any essential part in their development is debatable.

Ducts

In some sections of mammae affected with chronic mastitis, ducts are seen which are unlike the ordinary lactiferous ducts inasmuch as their epithelium is strongly eosinophilic and has other distinctive features; these appearances have been attributed to a metaplasia caused by oestrogen; if such an explanation is correct they must be included among the special concomitants of chronic mastitis.



Fig. 289.—From same source as Fig. 287. Shows papilliferous hyperplasia (× 100).

Cysts

The cysts of mastitis vary in size from those with a diameter of 1 or 2 millimetres to the large, discrete globular ones commonly described as "blue-domed". Some appear as if they had come into existence through enlargement and consequent tortuosity with kinking of the lactiferous ducts, whereas others, especially the large globular cysts, seem to have arisen from acini. The contents usually consist of a clear, glairy fluid, but this fluid may be brownish or greenish, or may resemble sebaceous matter or milk; occasionally the cysts contain blood, which indicates the presence of a papilloma or cancer. Within the cysts and dilated ducts collections of large, desquamated, globular cells may often be seen (Fig. 288). Usually the cysts are lined by a single layer of flattened or cuboidal cells though in advanced stages epithelial hyperplasia, papillae and cancer may develop within them.

4. CLINICAL PICTURE

Chronic mastitis is essentially confined to the reproductive period of life, and symptoms severe enough to cause complaint occur with increasing frequency from the age of about 30 years onward. During pregnancy and lactation the discomforts are relieved and at the menopause they permanently disappear.

The leading manifestations are a feeling of tension, pain, tenderness, ill-defined swellings and cysts of various dimensions. One or both breasts may be affected, and the signs may be limited to a single segment or even to part of a single segment; there may be 2 or more regions in the mammae in which the trouble is especially pronounced. In most instances the feelings of tension and pain are tolerable though they may be so severe as to cause a request for

mastectomy; but, whatever its degree, the pain is characterized by a variation in intensity at different stages of the menstrual cycle; it increases during the second half until a maximum is reached a few days before menstruation, at the onset of which, or shortly before, it rapidly declines. The pain is accompanied by tenderness which varies in degree in the same manner. It seems probable that the pain and tension may be attributed to the hyperaemia, oedema and secretory activity caused by progesterone in a breast already under the influence of oestrogen and affected with chronic mastitis. *Pain*

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Chronic Mastitis	*Cancer*
May be multiple foci and both breasts may be affected	Usually a single focus
Cyclical discomfort or pain may occur even at an early stage	Discomfort and pain are absent at an early stage
The breast is tender during the cyclical exacerbations of pain	No tenderness of breast
A swelling, if present, is not felt as a hard, discrete lump when palpated with the palmar surface of the fingers	The swelling is felt as a hard, discrete lump when palpated with the flat of the fingers
The skin is not adherent to the underlying tissue	The skin may be adherent
The nipple is not retracted	The nipple may be retracted
The mamma is freely movable on the pectoral fascia	The mamma may not be freely movable on the pectoral fascia
Axillary glands, if palpable, are not hard	Axillary glands, if palpable, are often hard

the presence of cancer. An increased temperature of the skin over the affected region, too, is a sign which does not help us to discriminate cancer from mastitis, for it accompanies both conditions.

Mazoplasia is a vigorous response of the mamma in early sexual life to the ovarian hormones, and it may be distinguished from chronic mastitis, not only by the early age at which it appears, but also by the absence of cysts and other evidence of that lesion. However, the two conditions are both caused by ovarian hormones, and it is difficult, and perhaps unnecessary, to define a strict boundary line between them. What began as mazoplasia may become a chronic mastitis with the lapse of years.

7. INDICATIONS FOR SURGICAL INTERVENTION

The need for operative treatment in chronic mastitis is exceptional. A reassurance as to the absence of cancer, with perhaps the wearing of a brassière, will usually provide all the treatment required, especially if there is a prospect of pregnancy or if the menopause is near. Subsequent examination at intervals is desirable so that cancer, if it supervenes, can be detected at a curable stage. Among the remedies which have been advocated are belladonna plaster, Scott's dressing, diathermy, cupping, inunction and massage, but these are hardly more than placebos. Massage is contra-indicated. For the treatment of mastitis by x-rays see the article on X-ray Irradiation for Non-Malignant Conditions.

Endocrinological methods

Until enough is known to enable us by endocrinological methods to regulate the output of ovarian hormones, we shall have little to offer the patient beyond reassurance and the prospect of a natural cure through pregnancy or menopause. Meanwhile testosterone has been found to give relief in many cases. To minimize general effects the drug should be applied to the breast as an ointment, and testosterone itself seems to give better results than testosterone propionate. The ointment is expressed from a collapsible tube, and the patient can regulate the dose by the length of the strip used. The daily dose varies from 4 to 10 milligrams, the measured length of ointment being rubbed into the affected breast for 15 minutes at bedtime (Spence, 1940). At first it may be necessary to apply the ointment regularly, but once the pain has been controlled its use may be confined to the few days of the menstrual cycle during which pain occurs.

Apart from such a minor affair as the aspiration of a cyst, the only indications for surgical intervention are (1) sufficient doubt about the diagnosis to necessitate a biopsy, and (2) unbearable pain.

8. OPERATIVE TECHNIQUE

Concerning biopsy little need be said except to emphasize the importance of removing sufficient tissue—tiny fragments are not enough for the foundation of an adequate pathological report, and if there is a "lump" this must be excised and not incised *in situ*. Care will, of course, be taken to render the scar as inconspicuous as possible, and it will, therefore, be situated as low down on the breast as may be compatible with the purpose in view. Deep sutures will be needed to prevent subsequent depression of the scar.

In those rare cases in which mastodynia has become so unbearable as to demand mastectomy, the extent of the operation will depend upon the extent of the disease. For removal of the entire gland the usual incision is a curved one corresponding with the sulcus formed by the lower margin of the breast and no skin is taken away. When the mamma has been dissected out one or more deep circular stitches are made to embrace the margin of the cavity and are drawn together so as to minimize subsequent scarring beneath the nipple and areola, and to avoid the otherwise possible and uncomfortable adherence of these structures to the chest wall.

(Figs. 286-289 *are from material provided by Dr. L. R. Woodhouse Price, of the Royal Cancer Hospital, and* Figs. 284-285 *are reproduced with kind permission from a paper by Wattenberg and Rose.*)

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[References to other titles are given under Breast—Chronic Mastitis in the Index Volume. The subject of Chronic Mastitis is also dealt with under the heading of Breast Diseases in the *British Encyclopaedia of Medical Practice* (1936), Vol. 2, p. 657.]

BREAST–INFECTIONS

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1. DEFINITION AND AETIOLOGY

80.] Pyogenic infections of the breast are most common during lactation; they sometimes occur during pregnancy and, rarely, at other times. Infection usually reaches the breast from the nipple, though rarely by the blood stream. Cracks at the nipple, combined with lack of cleanliness, are the most common cause. An indrawn nipple is also a most important aetiological factor.

Acute or chronic

Acute mastitis may resolve without suppuration, although frequently an acute abscess develops. A chronic pyogenic abscess is also a well-known clinical entity—both will be described in this article.

Tuberculous

Tuberculous mastitis is an important, but fortunately a rare, condition except in those places where tuberculosis is particularly prevalent. The infection is blood-borne but no special aetiological factor is known. The breast may be secondarily involved from tuberculous disease of the chest wall.

Actinomycosis very rarely involves the breast and then only as a spread from an intrathoracic infection.

2. MORBID ANATOMY AND BACTERIOLOGY

Acute mastitis with pyogenic organisms

The infection may occur: (a) in the subcutaneous tissues; (b) in the actual breast tissue; (c) in the retro-mammary tissues.

(a) The subcutaneous tissues

Infection in the subcutaneous tissues beneath the areola most commonly arises from infection in some of the sebaceous areolar glands, and readily proceeds to suppuration.

(b) The actual breast tissue

Infection in the actual breast tissue is the only true acute mastitis. During lactation it is not uncommon for one or more lobules of the breast to become engorged with milk as the result of obstruction to the ducts. An ideal culture medium then exists, and if the engorgement is not quickly relieved, suppuration takes place. To some extent, the fibrous interlobular septa prevent the infection tracking about freely, but in doing this they also do harm in that they increase tension, and much necrosis of the soft glandular tissue may result. Later the pus bursts through to other lobules so that a great area of the breast may be involved. These interlobular septa often cause a breast abscess to have a multilocular form. The organism found in nearly all breast abscesses is the *Staphylococcus aureus*; occasionally it is a streptococcal infection. In nearly all cases it is found to be penicillin sensitive. *Bacteriology*

(c) The retro-mammary tissues

Infection in the retro-mammary tissues, though occasionally of pyogenic origin, is much more frequently tuberculous. It arises from the chest wall, starting either in a rib or in an intercostal lymphatic gland. As the disease spreads, it involves the breast and may track through the substance of the organ, or more commonly points at its lower margin. Less frequently, tuberculosis starts primarily in the breast, the infection presumably having come by the blood stream. Sometimes caseation occurs with the formation of a cold abscess which soon reaches the surface: in other cases the response to tuberculous infection produces so much fibrous tissue that a hard mass is formed which resembles carcinoma. *Tuberculous infection*

3. CLINICAL PICTURE

A subcutaneous infection, usually from a subareolar sebaceous gland, appears as an inflammatory swelling, the diagnosis of which is obvious. When suppuration occurs fluctuation is readily obtained as the skin here is very thin. *Subareolar abscess*

(1) Acute mastitis

In adults the commonest time for acute mastitis to occur is in the first two months of lactation. As so often occurs during lactation one part of one breast becomes painful and hard, perhaps to subside in a few days without any special steps being taken. In other cases this hardness persists, causing great pain and there is some pyrexia. The condition may still subside without suppuration. It is often difficult to determine the exact moment when suppuration does actually take place, but the presence of oedema, a further rise in temperature, and the fact that the inflamed area takes on a more globular appearance all suggest suppuration. The discovery in the indurated area of a "spot" which is particularly red, hot, tender and soft indicates that there is pus deep to it, and of course fluctuation, if it occurs, makes the diagnosis certain. Fluctuation should never be waited for, but when the superficial part of the breast is first affected it may occur quite early. *Acute mastitis*

Acute mastitis in infants appears as a red swollen breast and the diagnosis is obvious. Sometimes it suppurates.

At puberty, in boys as well as girls, mastitis may occur. It very rarely suppurates and although its clinical appearance in boys is characteristic, quite often the condition is not recognized. The patient complains of slight pain under one or both nipples (it is frequently bilateral) and of a pricking feeling as though something sharp were sticking into him. A hard, circular, button-like mass, often with well-defined margins, is found.

(2) Chronic breast abscess

Chronic breast abscess is seen from time to time and is of particular importance owing to the mistakes which may be made in the diagnosis. Sometimes it dates from lactation and has remained since weaning, for months or even for years. Such an abscess may occur apart from lactation and may be due either to infection from a retracted nipple or to an infected haematoma; in other cases it may arise from suppuration in a galactocele.

The abscess if markedly chronic will appear as a hard, often painless mass with fairly well-defined edges and a smooth surface. In the less chronic type of abscess the mass is not so sharply defined nor so hard; it may be adherent to the skin or, if situated in the deeper parts of the breast, to the pectoral muscles; the skin may be oedematous (*peau d'orange*). Even in this type it may be impossible to obtain fluctuation owing to the very thick and tough fibrous wall, but Paget's test may be positive—the swelling being less hard in the centre than at the periphery. The axillary glands are usually enlarged, but are not very hard and may or may not be tender. The similarity of this type of breast abscess, therefore, to carcinoma, with the characteristic hard, painless, fixed lump and enlarged glands in the axilla, is very striking. In other cases when a less chronic condition obtains, one has seen a lump which fluctuates but is painless and thus simulates a cyst with chronic mastitis.

(3) Tuberculous disease of breast

The clinical picture of tuberculous disease of the breast varies according to the stage at which the condition is seen and according to whether it is a primary tuberculous mastitis or one in which the breast has been involved by spread of infection from the chest wall. Careful examination will usually make the latter condition clear because the breast with the mass in it will be fixed, not only to the pectoral muscles, but also to the thoracic wall itself. In the early stage of primary tuberculous mastitis one or more movable nodular swellings may be found in the breast, but usually the disease is seen in a more advanced stage, when there is a lump, perhaps somewhat tender, fixed to the surrounding breast tissue and perhaps to the skin (which may be purple coloured) or to the pectoral muscles. This lump has ill-defined edges and an irregular shape; it may closely resemble a carcinoma. Some cases are not seen until a later stage is reached, when caseation has taken place and the tuberculous pus has reached the surface, usually at several places. There are sinuses with indolent-looking granulations and an ill-defined, diffuse induration can be felt deep to them. At this stage enlarged glands can usually be felt in the axilla and sometimes these glands caseate and burst through to the surface. Affected persons are rarely in robust health and tuberculous lesions either old or active can usually be found elsewhere in the body.

(4) Actinomycosis

Actinomycosis of the breast does not occur as a primary lesion of that organ, but very rarely it may be involved by spread of infection from the chest. Unless the condition has advanced to that of sinus formation, with the discharge of yellow or greyish granules, there is nothing typical about the clinical picture by which the diagnosis may be made. The patient will probably already be known to have intrathoracic actinomycosis.

4. SPECIAL AIDS TO DIAGNOSIS

Comparatively little help can be obtained in the diagnosis of infections of the breast by special investigations. Some surgeons place a good deal of faith in a leucocyte count as being an aid to the diagnosis of pus, but it is safer to rely on clinical signs as a guide to making an incision in a breast abscess.

There is some difference of opinion regarding the wisdom of using an aspirating needle in breast swellings. In acute mastitis it should not be used for a number of reasons (*see under* Treatment). In chronic swellings it is sometimes tempting to explore with a needle to determine whether a lump is solid or whether it contains fluid (clear or turbid when a cyst is present; or pus in the case of a chronic abscess). Although there are exceptions to every rule, it is usually wiser not to needle a doubtful breast swelling. There is the danger that repeated needling of a carcinoma, in an endeavour to obtain fluid, may encourage dissemination. The pus in an abscess, as well as being thick, is difficult to find, and failure to obtain any fluid is likely to lead to a wrong diagnosis.

In an obscure chronic infection of the breast a skiagram of the chest should be taken to exclude pulmonary tuberculosis.

5. DIFFERENTIAL DIAGNOSIS

The most important point in differential diagnosis is to distinguish between carcinoma and either acute or chronic mastitis. During lactation, a carcinoma in a young woman may grow very rapidly, and this, combined with some tenderness of the lump and *peau d'orange* of the skin, makes diagnosis between it and an acute or subacute breast abscess most difficult; many of the other physical signs are similar, and in both there may be enlargement of the axillary lymph glands.

If the skin pits readily it is most probably an abscess, as the *peau d'orange* with a carcinoma is very firm. A little softening in the middle of the lump suggests an abscess. Well-marked pain, if present, and a leucocytosis also suggest an inflammatory condition.

With a chronic abscess the same confusion may arise, as it can simulate an ordinary carcinoma very closely. If a diagnosis cannot be arrived at an exploratory excision should be carried out.

6. TREATMENT

(1) Acute mastitis

The most important part of the treatment of acute mastitis is undoubtedly its prevention. In the later weeks of pregnancy some attention should be paid to the *nipples*, as acute mastitis most commonly arises from infection entering *Prophylactic*

through a crack in a nipple. Scrubbing with a brush and applying spirit has often been recommended but probably this does more harm than good by hardening the skin and making it more liable to crack. The best prophylactic measure is scrupulous cleansing with soap and water, a step which is all too frequently omitted; it is found to be most urgently necessary in the majority of patients admitted to any maternity hospital. Quite early in pregnancy retracted nipples should be drawn out, if this is at all possible, and subsequently kept out by repetition of this drawing-out process. Before and after each time the baby is put to the breast the nipple should be very carefully cleansed with sterile water or boric acid lotion.

Congested breast

If during lactation a painful hard area of congestion appears in the breast, heat should immediately be applied in the form of a kaolin poultice or radiant-heat lamp and the breast should be completely emptied, preferably by the baby. If this area of congestion is not relieved it is very likely to become infected. It is difficult to know when this occurs, but if, with the application of heat the congested breast does not rapidly improve, and the temperature rises, it is then wise to treat it as though it were infected and start systemic penicillin —15,000 units 3-hourly intramuscularly. There is no doubt that vigorous squeezing, handling or manipulation of the breast when in this flushed condition is harmful and leads to suppuration; such measures should be forbidden. The penicillin if started early is likely to arrest the development of the infection and prevent an abscess.

Infection

If, in spite of all these precautions, a breast abscess does form, it must be drained. Careful judgement must be exercised as to when this is done—the case will do better when a well-formed abscess is incised than when an incision is made into an area of inflammation. It is better to incise a day too late than a day too early, but this does not imply that one need wait for fluctuation. Aspiration of the abscess and injection of penicillin has been tried but only a few such cases recover without operation. A radial incision is made over the abscess, all pus is thoroughly evacuated and loculi felt for and opened up; if the abscess is in the lower part of the breast this incision will be sufficient—if the abscess is higher up, then a counter-drainage opening must be made below the radial incision. Local penicillin therapy should now be initiated. The upper part of the wound is sutured and a tube is put into the lower end of the wound, through which penicillin is injected 3 times a day. If the infection is severe, systemic penicillin should be administered as well. If penicillin is not available or this closed drainage with penicillin is not successful, a longer incision should be made into the abscess and ample drainage provided with the wound left widely open. The main cause of persistence of a breast abscess is an inadequate or badly placed incision.

Operation

Weaning

There is some difference of opinion as to whether or not a baby should be weaned when acute mastitis occurs. In the acute flushed breast there is no reason to wean, but, as already mentioned, the baby must be allowed to empty the breast completely, this being preferable to the use of a breast pump. When suppuration occurs, most surgeons prefer to dry up the breast by giving 15 milligrams of hexoestrol dipropionate; but a minority (and with them some experienced midwives) keep the baby on both breasts, even after the abscess has been opened, only taking it away if there is pus coming from the nipple, which usually is not the case. There is a lot to be said in favour of this

procedure from the mother's point of view, especially if the abscess has occurred in the first few weeks of lactation.

(2) Chronic breast abscess

As soon as a chronic breast abscess has been diagnosed it should be operated on. The abscess wall is usually very thick and if it is only drained, rather a large mass of tissue is left which forms a permanent lump; it is better therefore to excise the abscess entirely, and if this is done without opening it, the cavity left is obliterated with a few mattress sutures and the skin is closed. If the abscess is very large and chronic, a local amputation of the breast should be carried out. *Chronic breast abscess*

(3) Mastitis of infants

If pus is not present the breast area should be covered with a kaolin poultice. If an abscess occurs it should be incised and it usually heals without difficulty. *Mastitis of infants*

(4) Mastitis of puberty

Here suppuration is rare, and unless the pain is severe no treatment is called for. Whether occurring in a boy or girl the parent should be warned that it is quite likely to become bilateral. If there is much pain, heat may be applied but operation should not be considered. *Mastitis of puberty*

(5) Tuberculous mastitis

If one is fortunate enough to see such a case sufficiently early for the condition still to be a localized one, an excision of the affected area may wisely be carried out. In those more advanced and diffuse cases in which there are several sinuses, the whole breast should be excised, but it is not usually necessary to remove the underlying muscles. If the axillary glands are enlarged the incision should be extended upwards and outwards, and the edge of the pectoralis major defined and retracted upwards, exposing the axillary contents. The glands are carefully dissected away, care being taken of the neurovascular bundle to which the glands may be adherent. *Tuberculous mastitis*

If the breast has been secondarily infected from the chest wall, the affected area in the breast and pectoral muscles should be widely excised and the ribs exposed. *Tuberculous mastitis secondary to chest-wall infection*

By close examination of the chest wall a track will be found leading down to the diseased rib or ribs, and usually to their posterior surfaces through an intercostal space. However extensive the lesion in the rib or ribs the whole extent of diseased bone should be excised, and all tracks followed up and laid open; soft tissues which are evidently infected by tuberculous disease should be cut away. The wound is then closed.

7. RESULTS OF TREATMENT

An abscess in the breast, although it may be extensive and may appear to have destroyed much breast tissue, usually heals well, provided that it has been adequately dealt with. It leaves the breast looking a much more normal shape than might be expected, and a scar which is often surprisingly inconspicuous. Careful bandaging, to support the breast during the period after the abscess has been opened, contributes considerably to this satisfactory result. *Breast abscesses*

Provided the patient has no active tuberculosis elsewhere in the body,

Tuberculous mastitis

tuberculous mastitis should resolve well after complete excision of the infected area and primary healing of the wound. When the chest wall is the source of the breast infection, however, a more guarded prognosis should be given, as some outlying portions of the track are easily overlooked and the wound is slow to heal, or on healing leaves a sinus.

[References to other titles are given under Breast—Infections in the Index Volume. The subject of Breast Infections is also dealt with under the heading of Breast Diseases in the *British Encyclopaedia of Medical Practice* (1936), Vol. 2, p. 657.]

BRONCHIECTASIS

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1. DEFINITION

81.] By definition, bronchiectasis implies an abnormal dilatation of the air-tubes, but the clinical condition to which the term is applied assumes that infection has developed in the widened bronchi.

2. AETIOLOGY

A secondary condition

Bronchial dilatation is invariably secondary to some mechanical obstruction or inflammatory change affecting the air-tubes. Many theories have been suggested to account for production of the dilatation, ranging from a congenital weakness of the bronchial walls, traction on the walls as a result of surrounding fibrosis, excessive bronchial pressure consequent on cough, to softening of the walls following retained secretions. The most satisfactory current view is that bronchiectasis is associated with pulmonary atelectasis. Obstruction of



FIG. 290.—Specimen of lung removed for bronchiectasis. At the hilum is a large caseous gland. There are cystic changes in the upper lobe and saccular bronchiectasis in the lower.

Atelectasis a predisposing factor

an air tube by a foreign body, retained secretion or glandular pressure leads to rapid absorption of gases in the lung distal to the block. The alveolar tissues collapse and the previously air-containing section of lung is converted into a wedge-shaped mass of elastic-tissue fibres among which the air tubes retain their patency by virtue of their rigid cartilaginous walls. The tension and traction of this elastic tissue agglomeration leads to pulling over of the mediastinum, pulling in of the chest wall, elevation of the diaphragm and some degree of compensatory emphysema. But once the limits of these effects have been reached, the traction acts on the bronchial walls which must yield and be stretched. Re-ventilation of the collapsed lung may result in restoration of the normal bronchial lumen, but when the collapse persists a stagnant area remains: secretions collect and become infected in the course of time to produce a permanent condition.

Stagnation of secretions

Extra-bronchial and intrabronchial obstruction

Common causes of bronchial obstruction which, if unrelieved, may lead to bronchiectasis are inhaled foreign bodies (often unsuspected), glandular enlargement at the lung hilum as in tuberculous adenitis (part of the primary

tuberculosis complex) and whooping cough. In many forms of pulmonary inflammation purulent secretion, if not completely ejected, is another potential cause of atelectasis. Pus from infected nasal sinuses may readily be inhaled and it becomes a source of infection and collapse. The spread of *Purulent secretions* *Nasal sinusitis*

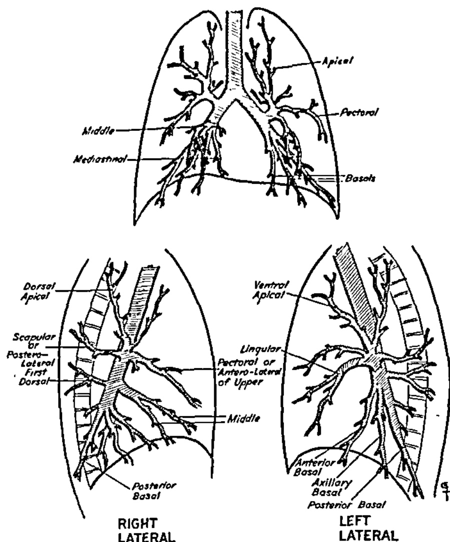


FIG. 291.—Anatomy of the bronchial tree.

bronchiectasis to adjacent segments of lung by "spill-over" may be explained by intermittent flooding of pus from infected into non-infected air-tubes.

Bronchiectasis occurs with great frequency in pulmonary tuberculosis, carcinoma and chronic suppurative diseases of the lung, but the main consideration has to be directed towards the primary condition. *Other conditions*

3. SURGICAL ANATOMY

An intimate acquaintance with the principal branches of the bronchial tree is essential to the study of this disease. The named divisions are indicated in accompanying illustrations, where it will be noted that on the left side the *Anatomy of the bronchial tree*

equivalent of the middle lobe is represented by a "lingular" branch off the upper lobe trunk.

Bronchiectasis tends to affect such air tubes as cannot empty their secretions readily under the action of gravity, such as the lower lobes. Secretions readily drain from dependent air tubes (upper lobes), and the infective element is minimal.

Types of dilatation

Terms such as saccular or fusiform suggest some of the varieties of bronchiectasis. It should be noted that the dilatation and distortion principally affect bronchi of medium size, but the abnormality is not usually visualized in terminal bronchioles which are probably occluded in the process of disease, nor is gross dilatation of the main lobar bronchi often seen. A false impression of dilatation is sometimes given in atelectatic areas where the air tubes are crowded and appear stumpy.



1 2 3 4 5 6 7 8 9 10 11 12

FIG. 292.—Specimen of lung showing gross cystic changes and thickening of all bronchial walls.

4. PATHOLOGY

In early uninfected cases there is little to detect microscopically in the affected lung. Without careful comparison, the degree of dilatation after removal from the body is difficult to assess. When obvious atelectasis is present there is a loss of alveolar pattern, with aggregation of elastic and fibrous tissue.

Parenchymatous and peribronchial changes

When infection is present there are signs of inflammation in the parenchyma and peribronchial tissues but the general bronchial structure is well maintained. The high ciliated columnar epithelium is more heavily stained and may show areas of desquamation, but it is most unusual to find gross ulceration of the actual bronchial wall. The epithelium has a lively power of regeneration. The lumen of the bronchi contains debris and purulent matter; lymphoid masses show enlargement, and round-celled infiltration is apparent in the peribronchial and adjacent tissues. An increase in fibrous tissue is apparent in the parenchyma which shows some loss of alveolar pattern.

5. BACTERIOLOGY

A voluminous and mixed flora in the secretion is common, occasionally with some preponderant pyogenic organism. Spirochaetes and fusiform bacilli are

sometimes found and are held to be responsible for foetor of the sputum. The bacteriological findings, however, have little bearing on therapy unless penicillin-sensitive organisms, such as the pneumococcus or the streptococcus, can be identified.

6. INCIDENCE

Literal interpretation of the term bronchiectasis would give a high figure to the incidence of the condition. Minor dilatations, of temporary character, may appear in any form of pneumonitis. Unless there has been a suggestion of lung disease during life, a moderate degree of bronchiectasis can easily be overlooked on routine necropsy examination. Many cases of "chronic bronchitis" reveal bronchiectasis if studied in detail. *Often undiagnosed*

The sex distribution is about equal and the age incidence shows that the disease predominates in childhood. Many cases are not diagnosed until adult life, though inquiry into the history may show that signs and symptoms were noticeable (and often wrongly diagnosed) several years previously. Bronchiectasis does occur in middle age and even in the elderly, but the progressive or infective forms usually result in premature death or severe ill health. *Age and sex incidence*

7. DISTRIBUTION

The lower lobes of the lungs are most commonly affected, and in about half the total number of cases only one side is affected. The left side is slightly more commonly affected than the right, and the disease is not necessarily confined to one lobe. Right lower and middle lobes, and left lower and lingular process, are common combinations. A bilateral picture of left lower and lingula with right middle suggests that the bronchi were affected by a general hilar gland enlargement. Bronchiectasis involving adjacent segments without affecting whole lobes probably results from pressure by glands of tuberculous origin. The whole lung may be affected, and in children this may take the form of a cystic dilatation with extreme fibrosis. *Local distribution*

8. CLINICAL PICTURE

The symptoms range from being almost negligible to those of gross toxaemia with indications of pulmonary inflammation. The classical text-book signs and symptoms are indicative only of very advanced bronchiectasis.

Cough and purulent sputum are the features which primarily bring bronchiectasis to notice. They are most marked in the early morning, when, after coughing up some yellow sputum, the patient may remain symptomless most of the day. Alteration of posture in more advanced cases will tip out secretions on to healthy bronchial mucosa and elicit the cough reflex. Young children usually swallow their sputum and, therefore, tend to mask the real condition, but coughing in the inverted position or gastric lavage may reveal pus which demonstrates the existence of the suppurative process. *Cough* *Purulent sputum*

Signs of chronic toxaemia are variable and in children manifest themselves in lassitude, unpleasant breath, poor appetite, dry flaky skin and lustreless hair. These children are listless and usually occupy a low position in school. *Toxaemia*

A history of repeated colds and coughs which "go to the chest" is common, and prolonged retention of secretions gives signs that are often confused with *Colds and coughs*

Haemoptysis

Recurrent pneumonia

pneumonia. Haemorrhage is an index of active ulceration, but is more often encountered in adults than children. Advanced signs include foetor, copious purulent sputum and obvious toxaemia with clubbing of the fingers. These, with recurrent attacks of pneumonitis, produce an almost intolerable condition, beyond the help of surgery.

Inconclusive physical signs

Physical signs in the chest vary with the state of the lung tissues and the amount of secretion in the dilated bronchi. In a dry case signs may be negligible, but usually slight dullness at the base close to the spine, harsh breath sounds and loud leathery râles, altering on coughing, are audible. These râles are easily conducted to the other side of the chest and should not lead to the hurried conclusion of a bilateral condition.



Fig. 293.—Bronchography. Injection of radio-opaque oil into the bronchial tree. In this instance the oil will gravitate into the right lower lobe.

Empyema

Cerebral abscess

Progress of disease

Pleural infection and metastatic abscesses are common complications, cerebral abscess being a fatal condition. Progress of the disease is almost inevitable after definite infection has been established. By "spill-over" bronchiectatic changes spread into adjacent bronchi and into basal tubes of the opposite side.

9. SPECIAL AIDS TO DIAGNOSIS

Radiology essential

The recognition of bronchiectasis can only be accurately established by radiology. The presence of much purulent sputum may suggest the condition, and an ordinary straight antero-posterior film may show lobar or segmental atelectasis; a uniform area of shadowing with traction of the mediastinum and chest wall towards this area, coupled with elevation of the diaphragm and increased clarity of adjacent lung tissue (compensatory emphysema), being the main features. Occasionally cystic spaces or even dilated bronchi can be detected on the skiagrams.

(1) Bronchography

Radio-opaque oil

The essential investigation for diagnosis is bronchography, which consists in the introduction of a radio-opaque iodized oil into the trachea, where, by posturing the patient, it can be induced to fill the required bronchi (Figs. 293 and 294). The oil used has a high viscosity which lets it adhere to the bronchial walls and not run too rapidly into the terminal bronchi and alveoli where it would obscure the x-ray picture.



Fig. 294.—Bronchography. Filling the middle and upper lobe on the right side.

(a) *Technique of bronchography*

Many techniques of bronchography have been advocated. One method in common practice is as follows:

Preliminary removal of bronchial secretions by means of prolonged postural drainage and coughing is carried out for several days before bronchography.

The actual procedure—most satisfactorily carried out on the x-ray table or couch—consists of making a subcuticular skin weal, with local anaesthetic,

over the crico-thyroid membrane, and then injecting 3 minims of 10 per cent cocaine or 2 per cent Nupercaine or amethocaine into the trachea with the same needle. The needle is rapidly withdrawn before the patient coughs. Next a wide-bore needle is pushed through the crico-thyroid membrane into the trachea. Opaque oil (such as Lipiodol or Neohydriol) is then injected into the trachea and the patient's position altered slowly so that the oil can gravitate into the lobes that are to be filled. Without undue delay lateral and antero-posterior films are taken, and if these are satisfactory the patient is allowed to cough.



FIG. 295.—Normal right bronchogram. Antero-posterior film. All branches are filled on one side only.

For adults 8 to 12 cubic centimetres is an adequate quantity (3 to 5 cubic centimetres per lobe), for children the amount should be reduced by one-half. Contrary to current opinion the oil should be used cold and not warmed.



FIG. 296.—Normal right bronchogram. Lateral film. All branches are filled on one side only.

(b) Unilateral bronchography

Casual bronchography is to be deplored since an initial failure will confuse later attempts. It should be the rule that bronchography is employed to fill only one side at a time. Films of lateral views are essential and are even more important than antero-posterior views. (Figs. 295–300.)

The opaque oil is, in part, coughed up but some inevitably descends into the finer bronchi and alveoli which were not filled at the



FIG. 297.—Antero-posterior film of bronchiectasis in the left lower lobe and lingular process. Note that it is almost impossible to differentiate the lingular process from the lower lobe without the lateral film.

time of bronchography. This residue obscures the x-ray films and, until it has diminished, delays performance of bronchography on the opposite side. The period of relative clearing is variable but averages from 2 to 3 weeks.

Not until a complete picture of both sides of the bronchial tree has been obtained can the extent and degree of any bronchiectatic changes be estimated. Occasional failure to fill affected bronchi may be due to their being filled with thick secretion on which the oil floats. In such cases, after further postural drainage and possibly bronchoscopy, the bronchogram can be repeated.

(*c*) *Bronchography in children*

A special note should be made about bronchography in young children. When co-operation is possible the procedure is performed under local anaesthesia, but if this is not practicable, general anaesthesia may be required and bronchoscopy is a useful preliminary to the actual injection of iodized oil. The amount of oil injected must be carefully gauged lest too great a quantity obstructs too many bronchi and virtually drowns the child. If a general anaesthetic has been employed postural removal of oil and secretions is essential once satisfactory x-ray films have been taken.



FIG. 298.—Lateral film of bronchiectasis in the left lower lobe and lingular process.

(2) Bronchoscopy

Bronchoscopy is used to exclude foreign bodies, bronchial stenosis, carcinoma and external pressure from enlarged glands. It can also show inflamed mucous membrane, purulent collections and the gross forms of dilatation. Routine bronchoscopy has much to recommend it.



Fig. 299.—Bronchogram showing right middle lobe bronchiectasis, lateral film.

(3) Tuberculosis

Exclusion of tuberculous infection is of the utmost importance. The Mantoux reaction, if positive, has no real significance but the absence of tubercle bacilli from the sputum can only be accepted after special culture methods or guinea-pig inoculation have proved negative.



Fig. 300.—Bronchiectasis, left lower lobe and lingular process.

(4) Associated naso-pharyngeal infection

The association of bronchiectasis with sinus infection is well recognized. Continual inhalation of infected matter from the nasopharynx may actually be causative of, as well as contributory to, the bronchial infection. Careful assessment of the accessory nasal sinuses may help in differentiating between genuine sputum from the depths of the chest, and inhaled or pharyngeal spit. Treatment of sinus infection may be required, but radical measures are not always satisfactory, possibly because the changes in the mucosa are allergic rather than infective.

10. DIFFERENTIAL DIAGNOSIS

Bronchitis
Phthisis

In the absence of bronchography, the dominant symptoms may lead to confusion with other chest conditions of which chronic bronchitis is an obvious example. Tuberculosis which produces constitutional signs and symptoms with sputum and haemoptysis is a common difficulty, and many cases of bronchiectasis are admitted to sanatoria every year.

Lung abscess
Cancer

Lung abscess with foetid sputum may only be differentiated by x-ray examination, and carcinoma of the lung or bronchial adenoma may produce a bronchiectasis the cause of which will only be recognized on bronchoscopy.

11. PROGNOSIS

(1) Progressive disease

The disease is essentially progressive. This applies particularly to bronchiectasis developing in childhood, when a symptomless condition may advance in several years to a hopeless condition of misery with widespread dilatation and toxaemia. The expectation of life is proportionately greater in cases in which symptoms develop in adolescence, and there are examples which are only recognized in middle or old age in the course of routine examination or investigation for mild chest symptoms.

(2) Regression

Regression of bronchiectasis has been very occasionally seen in childhood. Cases have been observed in which the dilatation in a collapsed pulmonary segment develops and then, if the lung re-expands, slowly resolves. A diagnosis of bronchiectasis must not be made on the relative widening of the tubes that occurs as they shorten in an atelectatic lung. This spontaneous resolution is, however, rare and must not be used as an argument for undue persistence with a conservative line of treatment.



FIG. 301.—Position for postural drainage of the lower lobes.

Bronchiectasis confined to a single lobe is a straightforward thoracic surgical problem; its extension even into a minor branch on the opposite side exaggerates the difficulties disproportionately.

12. CONSERVATIVE TREATMENT

(1) Postural drainage

Conservative measures to reduce toxaemia and symptoms are based upon postural drainage and breathing exercises. Postural drainage implies removal of secretions under the action of gravity and is achieved by placing the patient for long periods—hours not minutes—in such a position that the bronchi from the diseased area are dependent. As the disease is usually basal this means inversion of the patient, but other postures are needed if the disease is apical or in the middle lobe (Fig. 301).

(2) Breathing exercises

Active inspiratory efforts localized to the affected area are the basis for the breathing exercises which are so important in improving lung function.

(3) Septic foci

Teeth, tonsils and accessory nasal sinuses must be checked for sepsis as a routine, and may require treatment. Expectorants are not required if postural drainage is effective, and vaccine therapy based on sputum flora bacteriology is not helpful.

Routine bronchography every 12 months is advisable for observation of the condition, and may have to be performed sooner if there is any exacerbation of symptoms.

13. SURGICAL TREATMENT

(1) Pulmonary excision

Operative excision of the affected area of the lung is the only chance of producing a cure in bronchiectasis, but the removal of lung tissue must, of course, not be so extensive as to jeopardize the future respiratory function. A single lower lobe removal is the ideal indication. Association of lower lobe with a middle or lingular process, which occurs even more frequently, is also compatible with complete functional recovery. Removal of all lung tissue on one side—pneumonectomy—though a more severe procedure can give very good results. Removal of both lower lobes can also be considered, and also removal of left lower and lingula and right middle lobe, though, clearly, if bilateral operations are considered, the risks are greater and the functional end-result less satisfactory than if a less extensive removal is required.

(2) Pre-operative treatment

In assessing the prospects of operation complete and exact bronchography is essential, with close attention to septic foci elsewhere. A period of postural drainage and breathing exercises should be carried out before coming to the actual operation of lobectomy. Recently, the use of penicillin inhalations through a vaporizer or atomizer has helped to reduce the degree of infection in the sputum. It should be used if sensitive organisms are recognized.

14. TECHNIQUE OF LOBECTOMY

(1) Tourniquet or subtotal lobectomy

Lobectomy consists in freeing the affected lobe from all adhesions and securing the vessels and bronchus at the hilum of the lobe. Originally, the hilum was controlled by a snare tourniquet while the lung was cut away, and the resulting stump was sutured with mattress stitches to control vessels before the snare was released. This left a bulky mass of tissue, part of which inevitably sloughed, leading to a greater or lesser degree of pleural infection and the frequent formation of a bronchial fistula. Also, the amount of lung removed only entitled this form of operation to be designated as a subtotal lobectomy. A bronchus stump is inevitably left as a result of this procedure, and infection in this dead end is potentially dangerous.

(2) Dissection or total lobectomy

A more satisfactory elaboration of the operation is the isolation of each individual hilar vessel and bronchus. A total lobectomy—requiring, be it allowed, a higher degree of technical skill—is thus achieved and the incidence of sepsis greatly reduced.

Filling in of the "dead space"

The removal of a lobe leaves a dead space in the hemi-thorax which is filled up by compensatory emphysema developing in the remaining lung tissue. This process in an uninfected case, and particularly in children, is rapid, but if atelectasis of the remaining lobe occurs or if there is pleural infection the healing is delayed.

(3) Significance of pleural adhesions

Considerable controversy has ranged round the question of operating in a free or adherent pleura. The operation itself is more simple if there is a free pleural space, but the non-adherent residual upper lobe is more liable to infection if atelectasis occurs in it during the post-operative period. If atelectasis occurs, bronchiectasis may develop and become permanent, necessitating removal of this residual upper lobe at a later date. Also, if infection occurs in a free pleural cavity a total empyema will result, and the obliterating of the dead space, particularly at the apex, causes considerable delay in recovery.

On the other hand, if the upper lobe is held in position by adhesions, its re-expansion, even if atelectasis or infection in it should occur, is much less dangerous; also, if pleural infection develops, the condition to be treated is simply one of a localized basal empyema.

Therefore, the decision has to be made as to the merits of operating in a free or in an adherent pleural cavity. In recent years an adherent pleural cavity has been regarded as advisable, but with improvements in technique and with the use of penicillin to minimize infective complications, there is a tendency to consider operating in the presence of a free pleura.

An attempt to induce an artificial pneumothorax will demonstrate freedom or adherence of the pleural space. If this is free and adhesions are required, they may be produced by chemical irritation.

Artificial adhesions

Many methods and substances have been tried; the most satisfactory method has been found to be insufflation (over the upper lobe and apical pleura) through a thoracoscope of iodine (½ to 1 per cent) in talc powder. The air is removed completely and the pleuritis thus induced produces, within 3 weeks, firm but not too rigid adhesions between the visceral and parietal pleural surfaces. A few minims of strong silver nitrate solution (10 per cent) have the effect of inducing an obliterative pleurisy but not as constantly as with the powder. The reaction is often severe, accompanied by considerable pain. An effusion frequently results and this must be withdrawn completely to let the pleural surfaces come into apposition.

(4) Open pneumothorax

Anaesthesia constitutes a considerable problem since, with the wide open pneumothorax produced at operation, the mechanics of the thorax are markedly disturbed. Two basic factors have to be considered: first, maintaining adequate oxygenation with one lobe collapsed and the other lobe hampered by mediastinal displacement, and secondly, when operating in the lateral

position, the secretions of the diseased lung tend to gravitate into the air tubes of the sound side. These problems are countered by endotracheal anaesthesia with bronchial suction, by bronchus blocking, by controlled respiration, by posture, or a combination of these.

In cases with free secretion, our preference is to abandon the standard lateral posture and operate with the patient inverted, whereby the good lung is rendered safe and the mediastinum maintained in a central position (Fig. 302). Experience in thoracic anaesthesia is most necessary in handling these cases, and both surgeon and anaesthetist should be well accustomed to working together.

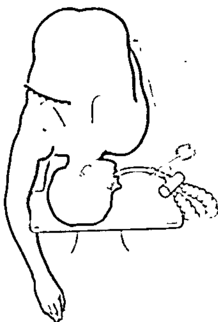


FIG. 302.—Position of patient and line of incision for lobectomy using the head-down or inverted posture.

(5) Lower lobectomy

(*a*) *Technique.* (*See* Figs. 303-309.) The chest is opened through a postero-lateral thoracotomy incision along the line of the sixth rib. Removal of this rib, or incision through the sixth interspace into the pleural cavity, is followed by widening of the incision with rib spreaders or retractors.

Adhesions

Adhesions are then freed, mainly by blunt dissection over the lower lobe. The interlobar septum which may be very incomplete is also identified. After the diaphragmatic surface of the lung has been freed, the pulmonary ligament is secured. Vessels of variable size may be encountered here and require ligation. Continuing along the relatively short length of the pulmonary ligament, the wide and thin-walled inferior pulmonary vein may be recognized and carefully isolated. Before attempting division, at this stage or later, this short vessel is controlled by double silk or thread ligatures (the Ballance stay-knot has many advantages). The lung edge is carefully freed from the lung root which may be enlarged by the presence of many inflammatory glands. These add to the difficulty of dissection. Deepening the interlobar fissure, one or two branches of the pulmonary artery will be identified and secured. Posteriorly, where the apex of the lobe lies at a higher level, the artery and bronchus to

Isolation of pulmonary vessels

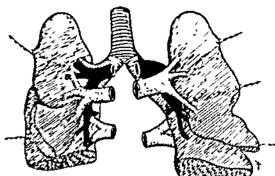


FIG. 303.—Anatomy of the pulmonary vessels. The length of the veins (stippled) is exaggerated. The arteries are black.

this segment are close together. Incision through actual lung parenchyma where the fissure fails may produce oozing which can be minimized by the judicious use of fine ligatures or sutures before dividing tissue. The order in which vessels are secured is not of great importance though, theoretically, arteries should be dealt with before veins. It is advisable to secure all strands of tissue anywhere near the hilum since oozing from minute vessels is undesirable.



Fig. 304.—Line of incision (6th rib) in the lateral position.

The bronchus

After division of all vessels the pedicle of the lung will consist of little else but the bronchus which is held in a control clamp while the lobe is cut clear. Closure of the bronchus is one of the problems of chest surgery and methods range from simple crushing and circular ligation to complicated use of intercostal muscle-grafts and pleural flaps. Careful occlusion with fine non-absorbable sutures and oversewing of adjacent tags of pleura or lung tissue is a common method.

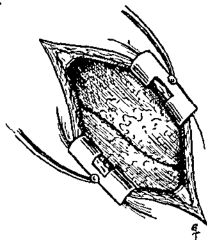


Fig. 305.—The incision is enlarged and the lung exposed. Note the fissure.

(*b*) *Closure of the thorax*

At the conclusion of the bronchus closure, penicillin and sulphathiazole powder may be dusted over the raw areas, and the lower edge of the upper lobe, if adherent, is freed for half an inch to allow compensatory expansion. The chest is closed in layers, using retractors to hold the separated ribs together while sutures are applied. Air is removed from the pleural cavity at the end of the operation.

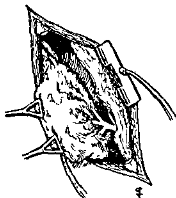


Fig. 306.—The affected lobe has been freed and the interlobar fissure incised to show the pulmonary arteries.



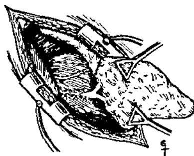


Fig. 307.—The base of the lobe is pulled up and after division of the pulmonary ligament the large inferior pulmonary vein is exposed and ligated.

15. AFTER-TREATMENT

(1) Aspiration of effusion

Some blood-stained effusion inevitably collects in the pleural cavity and should be aspirated within 24 or 36 hours, repeating the process at 1-day or 2-day intervals until the chest is radiologically dry. Each aspiration specimen should be examined bacteriologically to ensure early recognition of infection. In a satisfactory case, the specimens collected will remain sterile on culture, and the upper lobe expands to fill the dead space.



FIG. 308.—The lobar bronchus is isolated and clamped. Suture of the cut bronchus stump is followed by covering with a pleural flap or adjacent lung tags.

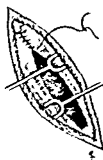


FIG. 309.—The ribs are approximated while the cut intercostal muscles are sutured.

(2) Expansion of residual lung

Insistence on coughing to clear the bronchi of any alien secretions which might lead to atelectasis is important, and, clinically, a freely moving chest betokens a healthy underlying lung. The use of posture and breathing exercises is valuable in maintaining normal ventilation and encouraging expansion of the residual lobe.

Within 3 or 4 weeks the chest should be filled and moving almost to the same extent as the normal side. (Figs. 310 and 311.)



FIG. 310.—Bronchogram following left lower lobectomy. The stump of the lower bronchus is just visible and there are bronchiectatic changes in the lingular process of the upper lobe.

16. COMPLICATIONS

(1) Empyema and bronchial fistula

Sepsis of the pleural cavity may occur in spite of chemotherapy, and is usually associated with the formation of a bronchial fistula. Early recognition of infection should be possible if each aspiration specimen is examined. In

the early stages daily aspiration may suffice, but if foul or bloody sputum is coughed up a fistula is indicated and drainage will be required. If drainage is instituted it should be maintained as a closed system with a water seal in the early stages. Later control of this dead space should follow the lines of empyema treatment.

Occasionally a severely infected case may be drained at the time of operation; this should be applied as a routine if the tourniquet technique is employed.



FIG. 311.—Bronchogram after removal of left lower lobe and lingula. Note absence of residual stump.

(2) Atelectasis

Atelectasis of the residual lobe is relatively common but can be relieved by immediate bronchoscopic suction. The relief is as dramatic as the onset when sticky mucus and pus is extracted from the bronchi.

(3) Pneumonia

Aspiration pneumonia is a complication affecting the opposite base which responds well to chemotherapy.

Breathing exercises

Breathing exercises and encouragement of movements and coughing minimize complications. The healing of a bronchial fistula is not always rapid and may take up to 3 or 4 months in some cases, but if carefully controlled its ultimate closure is certain. The only exception to healing occurs when tubercle bacilli are recovered from sputum or drainage.

(4) Tuberculosis

This complication accounts for a percentage of failures of lobectomy and is generally due to activation of the tuberculous process from trauma of unsuspected tuberculous lung tissue or latent hilar glands at the time of operation.

17. RESULTS

The results of lobectomy in carefully selected cases are excellent: the operative death rate is small and the proportion of cures high. In a series of 100 cases submitted to operation by the writer and his colleagues between 1939 and 1944, 6 patients died, but complete recovery with loss of symptoms was obtained in 83 cases. Of these lobectomies, 48 were single and 52 were multiple, but the question of single or multiple had little effect on the end-result. During this period the technique of dissection had not been brought to its present perfection, nor was penicillin available, but with the technique now employed and withpenicillin to assist in the prevention of septic complications,

a death rate of under 5 per cent and a recovery rate of 85 to 90 per cent may confidently be anticipated.

The distribution of the disease is given in the following table:

Distribution of bronchiectasis in 100 consecutive lobectomies

Left lower lobe and lingula - - -	35
Left lower lobe only - - - -	30
Right middle and lower lobes - - -	15
Right lower lobe only - - - -	9
Right middle lobe only - - - -	7
Right upper lobe - - - - -	2
Left upper lobe - - - - -	2

In the same period there were 15 pneumonectomies for involvement of all lobes on one side, and 4 bilateral lobectomies.

[References to other titles are given under Bronchiectasis in the Index Volume. The subject of Bronchiectasis is also dealt with under the heading of Bronchiectasis, Bronchiolectasis and Bronchial Spirochaetosis in the *British Encyclopaedia of Medical Practice* (1936), Vol. 2, p. 682.]

BURNS AND SCALDS

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1. DEFINITION

82.] A burn results from the action upon a surface of any of a variety of agents, such as excessive heat or cold, certain chemicals, and electrical currents. Cutaneous surfaces are commonly affected, but burns of the mucous membranes lining the mouth, nose, pharynx and upper respiratory passages can be caused by the inhalation of steam. A burn may be followed by local, or both local and general, manifestations.

2. AETIOLOGY

In civil life, the majority of burns are the result of accidents in the home, 90 per cent of which are avoidable. In a series of 1,803 cases (Brown,

Lewis-Faning and Whittet, 1945) treated in the Glasgow Royal Infirmary between June 1942 and August 1943, the injuries were sustained most frequently between 2 p.m. and 8 p.m., and the incidence of burns at a late hour was greatest in the early age groups. The chief agents in adults are fireplaces and hot water; in early childhood, cups of tea, kettles and fireplaces. The high incidence in poorer districts is linked with social and economic conditions. *Agents*

3. MORBID ANATOMY

(1) Classification

Burns are classified by extent and by depth. Berkow's table is used frequently to estimate the extent of surface lesions, but surface proportions vary widely between birth and adult life. Lund and Browder (1944) have evolved tables which make surface estimation of the area of burns more accurate at any age.

The four methods most commonly employed to classify burns by depth are compared in Table I. (*See also* Fig. 312.)

TABLE I

(Emergency Medical Services Memorandum, No. 8, 1943)

Dupuytren	German-American	Degree of Skin Destruction	Scottish
1st degree: erythema	1st degree		
2nd degree: vesication in the epidermis; vesication between epidermis and corium	2nd degree	Partial	Superficial
3rd degree: involvement of corium			
4th degree: involvement of subcutaneous tissue			
5th degree: involvement of muscle	3rd degree	Complete	Deep
6th degree: involvement of bone			

(2) Pathology

Living elements of the skin do not differ from other body tissues in their ability to withstand heat. Water between 50° C. and 60° C. with a duration of exposure of 1–5 seconds will produce erythema of the skin. If the duration is longer, a temperature of 51–52° C. will produce blistering although the subcutaneous temperature does not rise above 42° C. Recently, Mendelssohn and Rossiter (1944) have concluded that irreversible changes take place in the epidermal cells at temperatures between 45° and 52° C. With a duration between 1 and 5 seconds, temperatures between 85° C. and 100° C. produce vesication between the epidermis and the corium, and penetrate to the corium, and temperatures of 100° C., or above, destroy the entire depth of skin. In explosions, when the temperature is very high for a fraction of a *Effect of increasing temperatures*

second, a gaseous layer is produced under the epidermis which prevents further penetration of the heat; a superficial burn results. In complete destruction by flame, the skin is brown or black, leathery and insensitive; in destruction by scalds, it is dull white and slightly sodden.

Local effects Throughout the burned area the capillaries and venules are dilated and from them fluid escapes upon the surface, and also accumulates in the extra-

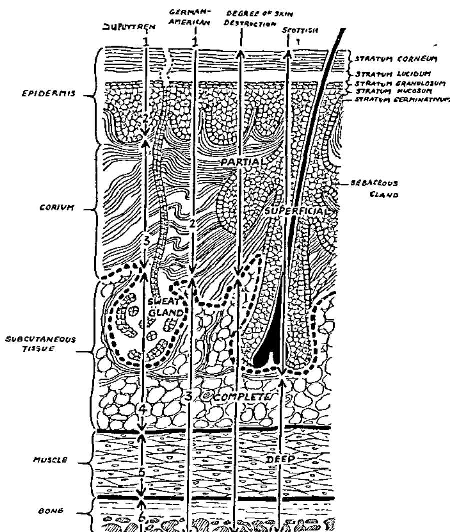


FIG. 312.—Classification of burns by depth.

vascular spaces, a condition which may last for 48 hours. The exudation of fluid into burned tissues is significant for two reasons: first, it is an important cause of shock; and secondly, its persistence delays healing and return of function. Work by Glenn, Peterson and Drinker (1942) has shown that sustained swelling in burned parts depends largely upon the deposition of coagulated exudate, which collects and holds a maximal amount of water delivered to the tissues from injured blood capillaries; the less the formation of coagulum, the less sustained the swelling and the quicker the healing.

Depth of burn In some instances it is difficult to tell the depth of heat injury. According to Clowes, Lund and Levenson (1943), the time when classification of burns by

depth should be made is after healing has occurred or successful grafting has been done. If the dermis is not completely destroyed, sufficient epithelial elements remain in sebaceous and sweat glands, and in hair follicles, to form a complete covering within three weeks. In deep burns a layer of granulations forms between living and dead tissue, and gradual separation of the slough takes place to leave a granulating surface. An epithelial covering grows in from the periphery: in large burns this process may take months and end in all manner of contracture deformities, with a thin, shiny, dry, hairless, irritable and unstable scar. Prominent scars are not infrequent.

Process of healing

Scarring

Burns are often compared with other injuries; "a burn should be regarded as an open wound due to heat" (Logie, 1944). This, however, is true only of superficial burns; deep burns resemble gangrene or massive death of tissue rather than a wound.

Where the subcutaneous tissue is scanty, heat from the causal agent may penetrate to the deeper tissues: thus in burns of the dorsum of the hands, tendons, tendon sheaths and joint capsules may be involved.

Systemic effects

When a large area of skin surface is involved, considerable systemic disturbances arise. In a few patients, an immediate state of primary or initial shock is demonstrable which resembles the vasovagal syndrome. In the first 12–24 hours there is often failure of the peripheral circulation—the condition of shock—as a result of the vascular changes in the burned area. It is now well established that the blood concentration and probably many of the shock-like symptoms in burns are due to leakage of plasma through the capillaries into the tissues at and near the burn, as well as into tissues remote from the injury. This results in a diminution of blood volume. To ensure adequate circulation to the heart and central nervous system, the reduced blood volume is redistributed by vasoconstriction in other organs. The blood changes accompanying these phenomena are increased viscosity and haemoconcentration, a shift of sodium and chlorides from plasma to cells, and of potassium from cells to plasma, a rise of non-protein nitrogen and a lowered carbon dioxide combining power. These changes may end in death from diminishing blood volume, falling blood-pressure and anoxia.

Loss of plasma

Biochemical changes

Blood-pressure

With the return of the capillary walls to normal, the oedema tends to subside and the haemoconcentration, blood-pressure and blood volume to return to normal.

Metabolic disturbances are indicated by a rising non-protein nitrogen content in the plasma, especially of the amino-nitrogen, hypoproteinaemia and increased urinary excretion of nitrogen. Loss of nitrogen in the exudate from the burned surface may also be considerable.

Metabolic changes

After the stage of shock there follows, in a small proportion of cases, severe constitutional disturbance resembling an acute intoxication. This stage is characterized by pyrexia, mental disturbances, albuminuria and tachycardia. The changes in the blood chemistry differ from those during shock: the fall of plasma proteins and the rise of blood urea are more pronounced, and the icteric index is raised. At necropsy degenerative changes of varying degree are found in all organs, and especially in the liver when tannic acid treatment has been used. Because of these findings, the name acute toxaemia is given to this stage. A final decision, however, has not been reached on the vexed question whether there is a non-bacterial toxaemia of burns.

Acute toxaemia

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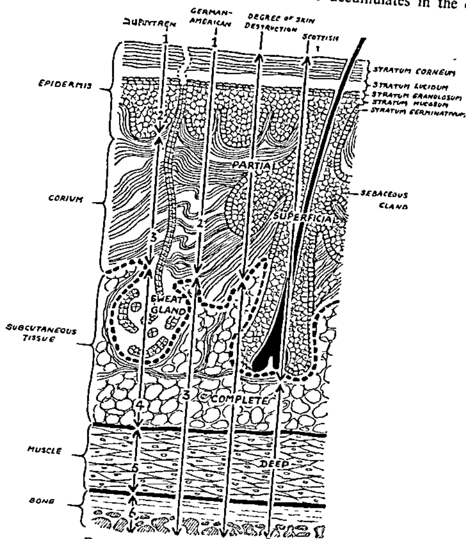


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Depth of burn

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leading to a diminished oxygen supply to important centres. Examination of the blood reveals a steadily increasing haemoconcentration. The patient becomes more restless and apprehensive, thirst becomes intolerable and persistent vomiting develops. In severe cases the exaggerated movements of air hunger appear.

Acute toxaemia The onset of acute toxaemia may be insidious or sudden, at any time between 6 and 60 hours after injury. Pyrexia is a constant feature; the skin and mucous membranes show a dusky or greyish cyanosis; vomiting occurs and the vomitus contains altered blood; the blood-pressure falls but is not associated with haemoconcentration if secondary shock is under control; the blood urea and icteric index are raised; the urine is scanty, dark and contains albumin, casts and bile pigment.

Septic toxaemia The stage of septic toxaemia is seldom seen with modern methods of treatment in superficial burns. Late blisters are a frequent source of infection, leading to pain, exudation of pus and systemic disturbances. In deep burns, infection, if it occurs, develops with the separation of sloughs and the patient exhibits the features of bacterial intoxication. If infection persists, emaciation and anaemia develop.

Healing The stage of healing in superficial burns is completed within 3 weeks by the growth of the epithelium from gland and hair follicle elements; in deep burns following the separation of sloughs a granulating area remains. Fibrosis takes place in the base of the granulations, and the area diminishes to allow a more speedy covering with epithelium growing in from the periphery. Since the covering is formed of thin, dry, shiny, hairless epithelium, it tends to be unstable and irritable. *Production of scar* The earlier a granulating area is covered with a skin graft, the less will be the underlying fibrosis and contracture deformity.

5. PRE-OPERATIVE MANAGEMENT

Objectives The chief objectives are to save life and to prevent or limit infection. These objectives can with advantage be put on a chronological basis (after Green, 1945) as follows: (1) to relieve pain, to relieve thirst, to prevent loss of heat; (2) to prevent invasion of the burn by pathogenic bacteria—in particular haemolytic streptococci; (3) to do no further injury to skin tissues which, though damaged, may still be viable; (4) to prevent or minimize plasma loss into the tissues around the burn and from the raw surface; (5) to counter "burn shock" by adequate intravenous "replacement therapy" with plasma or serum, and to attend thereafter to the correction of the metabolic disturbances which follow burning, by prescribing appropriate diet, and by other measures.

Control of vasovagal shock For the vasovagal or primary shock, the patient is covered with a sterile cloth, put to bed and wrapped in blankets. If available, a burn-reception room kept at an even temperature is used, or a specially made "burn caravan" or "tent" put over the bed. Artificial heating, however, unless carefully supervised and regulated can easily be overdone and become a source of great discomfort. In addition, vigorous heating may cause deterioration by inhibiting compensatory vasoconstriction. A safe plan would be to warm the chilled patient after starting the transfusion, but not before. Drinks of sweet tea or orange juice are provided. The pulse, temperature, respirations and blood-pressure are recorded and the blood concentration is estimated. If opium or morphine has not been administered previously, a suitable dose is given. (*See* Table II.)

(3) Bacteriology

Bacterial infection

Sources

Because of the relatively large raw area of damaged cells, extensive burns are easily infected. Infection may arise from many sources: the patient's skin or his upper respiratory passages; materials employed in first aid; clothing and blankets; the respiratory tract of surgeons, nurses or patients; the hands or instruments of dressers; and the infected air and dust of the wards. The presence of epithelial tags and of stagnant blister fluid tends to promote bacterial growth. The results of infection depend upon the virulence of the organisms, the resistance of the patient and the amount of necrotic tissue.

Bacterial flora

The bacterial flora is as a rule characteristic. Before treatment the *Staphylococcus albus* is often present. After first-aid treatment a variety of organisms may be observed: *Staph. aureus*, coliform bacilli, the *Bacillus subtilis* group, the enterococcus and sometimes haemolytic streptococci. Burns of the perineum, buttocks or thighs are frequently infected with coliform organisms.

In hospital, the organisms to be guarded against are haemolytic streptococci and *Staph. aureus*; usually they appear during the first week. In the second to fourth week, when sloughs separate in deep burns, mixed coccal and bacillary infections are frequent; the most common are coliforms, *B. proteus* and *Pseudomonas pyocyanea*. Sporing anaerobes are present infrequently. In the later granulating period the infections are mainly coccal.

(4) Special burns

Burns of air passages

Burns of the air passages may occur from the inhalation of flame or steam. In the upper passages, the lesions are found as a rule on the palate, fauces, epiglottis and hypopharynx, the surfaces of which are covered by thick mucus. After a few hours, the air passages become filled with frothy fluid which impairs the airway and therefore impedes gaseous interchange.

Electrical burns

Electrical burns can be divided into three degrees (Fisher, 1935): (1) reddening of the skin; (2) destruction of skin; and (3) destruction of the underlying tissues. The heat which produces these burns is much more intense than that producing ordinary thermal burns. The slough is deep and separates slowly by a process of aseptic necrosis. The local blood supply may be interfered with, so that late necrosis may develop.

4. CLINICAL COURSE

Stages in clinical course

The clinical course of an extensive burn may exhibit five distinct stages (Wilson, 1935): (1) vasovagal or primary shock; (2) secondary shock; (3) acute toxaemia; (4) sepsis; and (5) healing. Many burns exhibit only the stage of healing; others pass through each of the five stages in turn.

Vasovagal shock

Vasovagal shock arises immediately after injury and may last for 1–2 hours. It is characterized by a fall in blood-pressure, the patient feels cold and may complain of nausea, the pulse is of poor volume but slow, and haemoconcentration is absent. Spontaneous recovery takes place.

Secondary shock

Secondary shock begins as a rule between 30 minutes and 12 hours after injury. The patient becomes anxious and develops an insatiable thirst. The skin becomes pale or cyanotic, cold and clammy. The most characteristic feature is a progressive fall of blood-pressure. The first change is a diminution of pulse pressure; later both the systolic and diastolic levels are lowered,

leading to a diminished oxygen supply to important centres. Examination of the blood reveals a steadily increasing haemoconcentration. The patient becomes more restless and apprehensive, thirst becomes intolerable and persistent vomiting develops. In severe cases the exaggerated movements of air hunger appear.

Acute toxaemia

The onset of acute toxaemia may be insidious or sudden, at any time between 6 and 60 hours after injury. Pyrexia is a constant feature; the skin and mucous membranes show a dusky or greyish cyanosis; vomiting occurs and the vomitus contains altered blood; the blood-pressure falls but is not associated with haemoconcentration if secondary shock is under control; the blood urea and icteric index are raised; the urine is scanty, dark and contains albumin, casts and bile pigment.

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Healing

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Production of scar

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TABLE II

Opium Dosage for Burns and Scalds

A. In Children

Age	Preparation	Dose
1 month	Tinct. opii camph. (*B.P.*)	m. 2–3
2 months	Tinct. opii camph.	m. 4–6
3 months	Tinct. opii	m. $\frac{1}{4}$–$\frac{1}{3}$
6 months	Tinct. opii, *or* Inj. morph. sulph., *or* Inj. heroin. (diacetylmorphine hydrochlor.)	m. $\frac{2}{3}$–$\frac{3}{4}$ gr. $\frac{1}{150}$ gr. $\frac{1}{192}$
1 year	Tinct. opii, *or* Inj. morph. sulph., *or* Inj. heroin.	m. 2–3 gr. $\frac{1}{75}$ gr. $\frac{1}{96}$
1–3 years	Tinct. opii, *or* Inj. morph. sulph., *or* Inj. heroin	m. 2–6 + m. 2 in 15 minutes if necessary gr. $\frac{1}{45}$–$\frac{1}{35}$ gr. $\frac{1}{60}$
3–6 years	Tinct. opii, *or* Inj. morph. sulph., *or* Inj. heroin.	m. 6–12 gr. $\frac{1}{25}$–$\frac{2}{25}$ gr. $\frac{1}{48}$
6–11 years	Tinct. opii, *or* Inj. morph. sulph., *or* Inj. heroin.	m. 12–22 gr. $\frac{2}{25}$–$\frac{4}{25}$ gr. $\frac{1}{24}$
12 years	Tinct. opii, *or* Inj. morph. sulph., *or* Inj. heroin.	m. 24 gr. $\frac{1}{6}$ gr. $\frac{1}{12}$

B. In Adults

Age	Preparation	Dose
12–15 years	Tinct. opii, *or* Inj. morph. sulph., *or* Inj. heroin.	m. 30 gr. $\frac{1}{6}$ gr. $\frac{1}{12}$
15–20 years	Tinct. opii, *or* Inj. morph. sulph., *or* Inj. heroin.	m. 30 gr. $\frac{1}{4}$ gr. $\frac{1}{8}$
Over 20 years	Tinct. opii, *or* Inj. morph. sulph., *or* Inj. heroin.	m. 30 gr. $\frac{1}{4}$–$\frac{1}{2}$ gr. $\frac{1}{8}$–$\frac{1}{4}$

TABLE III

Atropine Sulphate Dosage

Up to 2 years – – – – – –	gr. $\frac{1}{200}$
2–5 years – – – – – –	gr. $\frac{1}{150}$
5–10 years – – – – – –	gr. $\frac{1}{100}$
10–12 years – – – – –	gr. $\frac{1}{100}$ – $\frac{1}{80}$
Adults – – – – – –	gr. $\frac{1}{100}$ – $\frac{1}{60}$

After the administration of the sedative the patient is left alone for 30 minutes. The blood-pressure and blood concentration are once again determined and the degree of shock is assessed. An estimate of the extent of the burn is made. The onset of secondary shock must be anticipated and if possible prevented. If it is already established or if the burn is extensive, a transfusion of human plasma or serum is set up immediately to restore the normal volume of circulating blood. *Control of secondary shock*

Various methods of calculating the desired dosage of plasma have been evolved. As a rough guide, when the blood-pressure readings are normal, one pint (568 cubic centimetres) of plasma is given within a space of 20 minutes, followed by a second pint at a slower rate. If after a period of 1 hour the blood-pressure readings remain normal, local treatment is begun. When the pulse-pressure is low, at least 2 pints of plasma are transfused rapidly (within a period of 20 minutes), after which the transfusion is continued at a slower rate. When the blood- and pulse-pressures are stabilized, local treatment may be begun, but slow intravenous infusion of plasma should be continued for at least 12 hours. Ogilvie (1944) issues a warning: "The shock of burns is not a temporary state that can be dispelled by the magic of plasma, leaving the patient safe for surgery or evacuation. Resuscitation restores the circulatory equilibrium, but the adverse forces continue at work for some time, and the patient needs re-resuscitation with more plasma at intervals for days." If large transfusions are required to restore the blood-pressure, the neck veins are scrutinized for over-prominence and the lung bases periodically examined. *Plasma dosage* *Massive transfusion*

From time to time clinicians have reported an improvement in circulatory collapse after extensive burns, following the administration of suprarenal cortical extract. The extract appears to exercise some effect over capillary permeability and the salt balance of the body. In extensive burns there is a considerable fall in the level of serum sodium which can be restored in some instances by the administration of desoxycorticosterone acetate; unfortunately there appears to be little or no effect on the capillaries. *Suprarenal cortical extract*

The second of the chief objectives is to limit infection. This may occur locally or in the respiratory tract. In extensive burns the early administration of penicillin systemically is the most valuable weapon available. In addition to limiting infection, it would appear to encourage the early separation of sloughs; this probably results from the growth of deep gland elements which brings about separation earlier than the digestive process of the leucocyte enzymes. Penicillin should be given intramuscularly in all deep burns, in all burns of the face and hands and in burns of the air passages either by a continuous drip method or intermittently every 3 hours. *Limitation of infection*

6. AIDS TO DIAGNOSIS

In many instances it is impossible to tell if the whole depth of skin has been destroyed. Recently, methods have been suggested to aid the recognition. Patey and Scarff (1944, 1945) apply van Gieson's stain (picro-fuchsine) to the raw area: the raw dermis without coagulation necrosis stains predominantly red, but with increasing amounts of necrosis it stains increasingly yellow. A standard method of haemoglobin estimation must be adopted, and the same observer must control the readings in a particular case. *Depth of destruction* *Haemoglobin estimation*

7. LOCAL TREATMENT

Additional objectives

The primary objectives in the pre-operative management—to save life and to prevent infection—still hold; intravenous therapy is therefore continued if considered necessary. There are two additional objectives: (1) to maintain or restore function, and (2) to restore a normal appearance.

Anaesthesia

Local treatment is embarked upon when the blood-pressure is stabilized. A preliminary injection of atropine sulphate is given (*See* Table III). Light general anaesthesia is recommended, preferably with cyclopropane, but if this is not available, gas and oxygen, supplemented if necessary with ether is used. Some workers avoid inhalation anaesthesia and employ scopolamine and morphine by injection. Though this limits the tendency to increased shock associated with inhalation anaesthesia, there is the danger associated with the employment of powerful respiratory depressants.

Principles in treatment

The principles in treatment can be summarized: (1) to prevent the risk of infection or re-infection of the burns in hospital; (2) to eliminate pathogenic organisms already present on the burned area and surrounding skin, without doing further injury to viable tissues ("plenary treatment"); (3) to control local oedema around the burn; (4) to allow free movement as soon as possible after 10 days; (5) to prevent deformity by preparing the burned area for skin grafting as soon as possible, unless the burns are so small and so situated that satisfactory natural healing within 21 days can be expected; (6) to assist the separation of sloughs and treat streptococcal or other infections which may be delaying skin grafting; (7) to treat the protein deficiency, anaemia and cachexia which may follow severe burns, especially those heavily infected in the sloughing stage; (8) to ensure satisfactory rehabilitation of the patient, and provide any necessary follow-up treatment, including x-ray therapy for keloid, and plastic surgery to restore function and appearance.

Plenary treatment

Before cleansing, swabs for culture are taken from the burn and the surrounding skin. The cleansing or "plenary" treatment is carried out in a warm operating theatre or specially devised burn-caravan. Precautions are taken as for a major surgical operation. Cap, mask, gown and gloves are worn by the surgeon, and the burn is treated in sections to avoid prolonged exposure. Speed is combined with gentle thoroughness. The surrounding skin and then the burn are cleansed with 1 per cent Cetavlon. Cetavlon is a synthetic detergent, cetyltrimethylammonium bromide, which apparently reaches the organisms in the depths of the sweat and sebaceous glands and hair follicles; it has a rapidly lethal action on haemolytic streptococci. The Cetavlon is applied by swabs which, with gentle sweeps from the centre of the burn towards the perimeter, wipe off the raised epidermis. Special attention is paid to the edges where all loosened epidermis must be detached. The Cetavlon is washed off with saline and the burn dried with gauze or with the warm air current of a hair drier. If Cetavlon is not available the plenary treatment is carried out with gauze wrung out of white soap solution or warm normal saline.

Cetavlon

(1) Pressure dressings

Advantages

For five years the writer has employed this method of treatment and found it the most generally applicable and successful. The advantages are: (1) the patient is comfortable; (2) in superficial burns healing has taken place by the first dressing; (3) oedema is limited; and (4) return to function is early.

Cameron and his colleagues (1945) have demonstrated that delay in the application of pressure detracts from the advantages. The disadvantages are: (1) experience of the details of the method is required; and (2) careful attention is demanded for 48 hours. *Disadvantages*

Some authorities consider preliminary plenary treatment unnecessary, but most consider the step beneficial. The burn is covered by gauze spread with soft paraffin, Vaseline, a sulphonamide cream (see p. 528), or a 5 per cent emulsion of sulphathiazole with triethanolamine is employed. The dressing is covered with gauze and wool, and fixed with crêpe bandages to ensure even pressure. Needless to say, the compression must provide moderate tension only, it must be uniform and it must not cause constriction. A plaster slab —not an encircling plaster bandage—is then applied to ensure immobilization and to render elevation of a limb, for example, easier. The initial pressure dressings are not disturbed for 14 days, by which time superficial burns are healed, whereas deep burns require removal of sloughs prior to grafting. Cultures are taken from any raw area. *Method*

(2) Coagulation treatment

Coagulants are applied in solution or as jellies. A coagulum is formed by the precipitation of the proteins of the exudate and surface cells. The intact epidermis is not affected. The advantages of coagulation treatment are: (1) external fluid loss from the burned surface is minimized; (2) treatment is painless; no dressings are required; in superficial burns with the separation of the coagulum healing has been completed; granulating surfaces are well formed in deep burns. The disadvantages of the coagulation treatment are: (1) sloughs separate slowly; this is a distinct disadvantage in deep burns where skin grafting must be carried out as soon as possible; (2) in burns of large surface area, the coagulum is difficult to keep intact and dry, especially at the flexures; once infection gets under a coagulum the results are serious; (3) the possible constricting effect of an encircling coagulum on a burn of the extremities; coagulants should be avoided in burns of the hands and face. *Advantages* *Disadvantages*

(a) *Silver nitrate*

The writer has found this coagulant successful in the treatment of extensive scalds in children. Following completion of the plenary treatment, the scald (and the surrounding skin) are painted with 0·5 per cent crystal violet, 0·1 per cent proflavine or 1:500 brilliant green, and dried. Silver nitrate solution (10 per cent) is then applied by means of a gauze swab; the healthy skin is not touched. The surface is dried and a second coat of silver nitrate applied. The patient is returned to bed and nursed in whatever position permits satisfactory after-care with comfort. The coagulum is exposed by nursing on the unaffected side; affected limbs are elevated. The coagulum is inspected three times daily; cultures are taken from moist areas. All late blisters are snipped and an antiseptic and silver nitrate applied in turn; cracks and fissures in the coagulum are similarly treated. If the patient is burned back and front, he is nursed on the less affected surface, which is protected by sterile towels or by gauze covered with a coagulating jelly. In superficial burns, following the complete separation of the coagulum in about 14 days' time, a thin smear of cold cream, boric ointment or lanolin is applied. If the coagulum is adherent *Choice of coagulant* *Care of coagulum* *Separation of coagulum*

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which should be scrutinized in 3 or 4 days. If necessary the cream is re-applied. Recently, a cream containing 3 per cent of sulphathiazole and 200 units of penicillin per gramme has been used.

(4) Occlusive membranes

Many types of occlusive preparations have been suggested. The more recent examples include fibrins containing sulphonamides with various plasticizers, for example, the spray of sulphadiazine with triethanolamine and methyl cellulose (Pickrell, 1942); sulfafilms (Dingwall and Andrus, 1944); medicated Cellophane (Farr, 1944); medicated gelatin (Roback and Ivy, 1944); coagulated plasma or serum (Macfarlane, 1943; Miscall and Joyner, 1944; Rabinowitz and Pelner, 1944); fibrin films from human fibrinogen and thrombin (Hawn and his co-workers, 1944); sheets of dried plasma containing sulphonamides (Pollock, 1944); and casein films (Curtis and Brewer, 1944).

(5) Saline dressings

Advantages The advantages of the method are: (1) movement is encouraged from the first—by some this is not considered to be an advantage; (2) sloughs separate early. *Disadvantages* The disadvantages are: (1) it does not prevent or limit fluid loss; (2) it involves frequent changes of dressing, and exposure of the burn to bacterial contamination; (3) considerable nursing personnel are required; and (4) sharp reactions are sometimes experienced.

Method of application After plenary treatment the burn is covered with tulle gras or any meshed gauze coated with soft paraffin, and with gauze wrung out in warm normal saline. The saline dressings are repeated 4-hourly, the tulle gras changed once daily. A sulphonamide powder is dusted on to the surface of the burn.

(6) Saline baths

Method of use In some hospitals a constant-temperature saline bath has been installed. After sterilization of the interior of the bath, it is filled with normal saline at 100° F. At intervals of one minute an automatic feed delivers additional saline at the required temperature and concentration. In addition to the burns, the surface of the bath is examined bacteriologically twice a week. When the patient is immersed, loose tags are removed and the separation of sloughs encouraged.

(7) Envelope treatment

The advantages are similar to those enumerated under saline dressings. The disadvantages are: (1) it does not prevent or limit fluid loss; (2) the tissues may become sodden, and may show chemical irritation; (3) splinting may be necessary to prevent deformities.

Method of application Plenary treatment is carried out with a 5 per cent solution of electrolytic sodium hypochlorite at 100° F. If the burn is on the extremities, the nails are cut short. A suitably shaped envelope is then applied, made of silk rendered watertight by a coating of synthetic resin. A strip of adhesive plaster seals the proximal end of the envelope to the shaven skin.

8. SPECIAL BURNS

(1) Eyelids and eyes

Eyelids In burns of the eyelids, coagulants, if applied, may lead by their "splinting" action to "exposure keratitis" and perhaps to the loss of a previously uninjured eye. A smear of Vaseline or cold cream to the eyelids is all that is usually

after 3 weeks, then the skin underlying must be considered lost. Separation of the coagulum is encouraged by the 4-hourly application of hypertonic saline (3 per cent) soaks: for the same reason intramuscular penicillin should be administered. In some instances, it is wise to excise the coagulum along with a quarter of an inch of the surrounding skin, and apply a thick razor or dermatome graft to the defect.

Infection under coagulum

If infection occurs beneath a coagulum, a window is cut to permit the escape of pus, and steps are taken to encourage separation.

(*b*) *The dye antiseptics*

The dyes help to control bacterial infection, and at the same time form a thin coagulum or crust. They have therefore, up to a point, the advantage of silver nitrate but, at the same time, all the disadvantages. The dyes in common use are crystal violet 1 per cent, brilliant green 0·002 per cent, and members of the acridine group. A popular variety is triple dye, mixture of gentian violet 2 per cent, brilliant green 1 per cent, and euflavine 0·1 per cent, in equal parts.

Dyes in use

(3) Local sulphonamides and penicillin

Advantages

Disadvantages

Many methods of applying sulphonamides locally have been employed, such as in powder or in a cream or paste. The object is to eliminate infection, especially by haemolytic streptococci. The advantages claimed are: (1) no general anaesthetic or special equipment is required; (2) the patient is comfortable; (3) re-dressings are simple. The disadvantages are: (1) it does not prevent fluid loss; (2) it does not control infections by coliform bacilli, *B. proteus* or *Ps. pyocyanea*: (3) the policy of infrequent dressings inevitably entails a certain amount of odour, and this in turn attracts flies (Medical Research Council, 1944).

Sulphonamide cream

A pre-operative injection of morphine is given. After plenary cleansing with 1 per cent Cetavlon, a bland antiseptic cream similar to the following is applied:

Sulphanilamide	3 grammes
Sulphathiazole	3 grammes
Glycerin	10 grammes
Castor oil	25 grammes
Lanette wax SX	10 grammes
Water	49 grammes

The cream is prepared as follows: Heat 25 grammes of castor oil to 70° C. and add 10 grammes of Lanette wax SX. When the wax is completely melted, add 49 grammes of water previously heated to 65° C. with gentle stirring to avoid incorporation of air. Heat the whole to 100° C. for at least 30 minutes to kill off non-sporing pathogens, and shake as it cools. Rub up the sterile sulphanilamide and sulphathiazole powders, 3 grammes of each, in a sterile mortar with 10 grammes of glycerin. Heat to 65° C. for 2 hours and then mix slowly with the base. Store in a sterilized jar and always keep covered. When the cream is to be kept for a long period, 0·2 per cent chlorocresol may be added as a preservative. The cream is applied to the burn on sheets of gauze, and firm pressure is secured by wool and crêpe bandages. The first dressing is carried out in 6–12 days' time, except in burns of the hands, and the areas around the mouth and nose, and of the buttocks, perineum and genitalia,

(5) Chemical burns

All contaminated clothing is removed. The affected part is washed with a copious stream of water.

(a) Lime

All particles must be wiped away or removed with instruments, then the part flushed with water or weak acetic acid. Before removing lime particles from the eye, a drop of a mixture of equal parts of tincture of opium and distilled water is applied. Thereafter a 1 per cent solution of atropine sulphate is dropped in twice daily and liquid paraffin 4-hourly. To prevent symblepharon, a glass rod drawn out into a bulbous end is well coated with Vaseline or atropine ointment, and the bulb swept round the upper and lower fornices. According to recent observations, drops of 15 per cent sodium sulphacetamide, by limiting secondary infection, have lowered the incidence of adhesions.

(b) Nitric acid

Roberts (1941) reported an excellent result by rubbing with chlorine (eusol) solution.

(c) Caustic soda

In factories in which burns with caustic soda are liable to occur, a wise precaution is to keep a 5 per cent solution of ammonium chloride at hand. The affected surface is irrigated immediately with this solution; a burn will be prevented if this is done within 30-40 seconds of contact. If a burn is caused, its severity is very greatly lessened by the irrigation. In burns of the eye, irrigation is carried out with 5 per cent ammonium chloride solution, followed by warm boric-saline lotion for 1 hour.

(d) Phosphorus

Phosphorus burns are limited mainly to war-time and therefore will not be discussed here.

9. AFTER-TREATMENT

(1) Immediate

This refers to the healing stage. To stimulate healing, blood transfusions, protein infusions, high protein and salt diets may be advantageous. Where there is loss of skin, grafting is necessary. Once healing is established, the aims are to mobilize all scars and to encourage free movements of all joints in the neighbourhood. Special physiotherapeutic measures are adopted to counter oedema still present, such as massage, wax baths and so on. Wakeley (1942) suggests massage of the burn with lanolin each night (Ung. lanae co. *B.P.*) for the first 3 months. Prolonged exposure of the healed burn to the direct rays of the sun is to be avoided. *Value of transfusions* *Massage, wax baths*

Superficial x-ray therapy is of considerable value in reducing keloid formation in its early soft vascular phase; in late phases, and after the scars have become pale and hard, the results of x-ray therapy are disappointing. *X-ray therapy for keloid*

(2) Late

This refers to the later problems, such as rehabilitation of the patients and plastic treatment.

During the war years many rehabilitation centres were established. Opinions *Rehabilitation*

Eyes

necessary in superficial burns. Burns of the eye may lead to: (1) injury to the cornea; and (2) injury to the conjunctiva resulting in simple conjunctivitis, conjunctivitis with exudate, or conjunctivitis with necrosis. In such cases, interference with the limbal circulation may lead to the formation of secondary opacities in the cornea. Siegel (1944) advocates early grafting with mucous membrane where there is damage to the perilimbal circulation. Conservative

Treatment

treatment consists of irrigation of the conjunctival sac with normal saline or tepid water, followed by the instillation of a few drops of cocaine hydrochloride. Drops of sodium sulphacetamide 15 per cent, or penicillin, are beneficial.

In burns by acids and alkalis at least 200 cubic centimetres of irrigation solution are used. Thereafter 1 per cent solution of atropine sulphate is dropped in twice daily, and liquid paraffin 4-hourly.

(2) Face

Where the burn extends into the scalp, the hair is shaved for at least 2 inches beyond the burn. If this is not carried out, infection will undoubtedly

Penicillin

supervene. As indicated previously, systemic penicillin is administered. After local plenary treatment, saline dressings are applied over tulle gras. The saline dressings are repeated every 4 hours, the tulle gras once daily. Superficial burns heal quickly; in deep burns the separation of sloughs is carefully watched, and when all sloughs have separated skin grafts are applied.

(3) Hands

Features of skin of hand

The most distressing problem of war burns is the burned hand. The skin of the hand is very vascular and if the burn is superficial and remains clean, healing is speedy. The thick epidermis on the palmar aspect gives good protection. Any blister on this aspect is snipped and pressure is applied to encourage its re-attachment. In all deep burns of the hands, skin must be grafted as soon as possible to avoid contracture deformities. Systemic penicillin is administered.

Pressure dressings

Detailed treatment

The treatment adopted by the author is that of pressure dressings. The hand is cleansed with 1 per cent Cetavlon or soap, and the nails are cut short. After 5 minutes a second wash is given. With a Vaseline bandage each finger is bandaged in the position of function, evenly and carefully; the bandage is continued over the hand and wrist. Liberal quantities of wool are then applied and fixed with a crêpe bandage to maintain light even pressure. To render elevation easy and to ensure immobilization, a plaster slab is added. The dressing is left for 12–14 days; by that time superficial burns are healed—deep burns will require a further 10 days of rest, and then grafting.

(4) Air passages

Oxygen administration

Treatment of these is unsatisfactory. Oxygen is given continuously by the oro-nasal type of B.L.B. mask. To get the maximal possible saturation of capillary oxygen and partial pressure, a concentrated flow is required of 6–7 litres per minute. If laryngeal obstruction develops, tracheotomy is performed at an early stage. Repeated spraying of the upper passages is carried out with 30 per cent glycerin in water. Penicillin is administered as prophylaxis against broncho-pneumonia.

Penicillin

11. RESULTS

Provided secondary shock is prevented or controlled by adequate fluid replacement, the results in superficial burns following modern methods of treatment are good.

In deep burns, however, there is too great a tendency to permit sloughs to follow their natural course of slow separation, and to allow the epithelium to grow from the edges, rather than to adopt more radical procedures such as excision of dead tissue followed by grafting. Early grafting must be the aim in all deep burns.

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vary as to the best form of rehabilitation: the nearer the approach to the patient's own work, or to some occupation which keeps his mind and hands continually employed, the better.

Plastic treatment

The details of the early and late plastic treatment of burn scars and ulcers will not be considered, though the surgeon controlling a burn unit must be conversant with all forms of plastic procedures.

10. PROGNOSIS

The prognosis depends upon a number of factors (Pack and Davis, 1930), as follows: (1) the nature of the burning agent; (2) the age, sex and occupation of the patient; (3) the extent of the body surface affected; (4) the depth of the burn; (5) the site of the burn; (6) the presence or absence of complications.

In Wilkinson's (1944) series in children, the mortality in 298 cases of scalds was 3·7 per cent and in 68 cases of burns 10·3 per cent. In children, extent is more important than site and depth, since the ratio of surface area to body weight is greatest at birth and gradually decreases. In a statistical analysis of 1,803 cases of burns (Brown, Lewis-Faning and Whittet, 1945), the incidence was higher at the younger ages, but the results were more serious in older patients. The incidence was higher in males but the mortality greater in females. Erb, Morgan and Farmer (1943) have published an account of 61 cases of fatal burns, all examined by the same pathologist between the years 1920 and 1942; of 41 treated with tannic acid 25 showed definite hepatic necrosis at necropsy whereas this lesion was completely absent in 20 untanned patients. Their records bear out the great reduction in the mortality of burns after tannic acid was first used in 1925—from 32·2 per cent to 11·8 per cent—but they add that the introduction of sulphonamides and other methods have further reduced the mortality. An additional fact demonstrated by their figures is the transfer, after tannic acid treatment, of the main mortality from the period of shock (12–36 hours) to the period of toxaemia (3–6 days), the time when the necrotic lesion in the liver is most often found. From recent observations the toxaemia results from the absorption of local applications such as tannic acid (or impurities therein) to the burn. Similarly, other local applications, for example, sulphonamides, may be absorbed in excess from extensive burns and give toxic symptoms. Burns are more serious in children. The site of the burn influences the prognosis: burns of the face, groin and flexor surfaces are serious.

TABLE IV

MORTALITY FROM BURNS IN GREAT BRITAIN AND IN THE UNITED STATES OF AMERICA

	SCOTLAND 1937	ENGLAND AND WALES 1937	U.S.A. 1939
Population - -	4,976,610	41,031,000	128,000,000
Deaths from burns -	256	1,318	6,240
Death rate per 10,000	0·51	0·32	0·49

II. RESULTS

Provided secondary shock is prevented or controlled by adequate fluid replacement, the results in superficial burns following modern methods of treatment are good.

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infection from sepsis in the hand and forearm. Chronic serous bursitis is almost an occupational disease, two well-known varieties being the "student's" elbow and the "miner's elbow" (Fig. 313). Lastly, it may be the seat of gouty deposits, sometimes of great size.

The ischial bursa covers the tuber ischii and is of relatively little importance. Chronic enlargement is usually bilateral and is traditionally associated with prolonged sitting, hence the term "weaver's or tailor's bottom". In earlier days a gummatous bursitis was well recognized.



Fig. 313.—Bilateral olecranon bursitis; the "student's elbow" or "miner's elbow".

The gluteal bursa lies between the tendon of the gluteus maximus and the great trochanter of the femur. It is occasionally affected by tuberculosis but is otherwise rarely met with in surgical practice.

The prepatellar bursa strictly speaking does not lie in front of the patella but is anterior to the ligamentum patellae and overlaps only a very small segment of the patella (Fig. 314). Lying as it does immediately beneath the skin it is most vulnerable to all types of injury and is, therefore, more commonly affected by disease than all other bursae, so that "housemaid's knee" is the classical type of chronic serous bursitis. It may readily be infected either by direct implantation, local spread or by lymphatic drainage from a distant focus usually on the toes or foot.



Fig. 314.—An enlarged prepatellar bursa.

Two small bursae are related to the tendo Achillis, one superficial, covering the insertion into the os calcis, another deeply placed between tendon and bone. Each may suffer chronic enlargement as the result of pressure from ill-fitting shoes.

(2) Bursae communicating with joints

The semimembranosus bursa lies between the tendon of this muscle and the inner head of gastrocnemius and has a narrow opening into the postero-internal aspect of the knee joint. Its enlargement, therefore, may be secondary to disease of that joint, which must be excluded before an excision of the sac is contemplated. Primary disease of this bursa is limited to a chronic serous bursitis, particularly in children. It may be bilateral, and in these cases the opening into the joint appears to have been sealed off, since no demonstrable communication exists.

The popliteus bursa has so large an opening into the joint that it is rarely, if ever, enlarged except as a result of disease of the knee.

The psoas bursa lies between the psoas tendon and the capsule of the

BURSAE

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1. DEFINITION

83.] Bursae are of three varieties. True bursae are interposed between two moving surfaces to reduce friction or are placed over prominent bony points to act as protective cushions. Bursal extensions of joints fulfil a similar function but are continuous with the synovial membrane of the joint. Adventitious bursae are developed where bony prominences are subjected to sustained pressure. In structure, all bursae consist of a fibrous capsule lined with endothelium analogous to the synovial membrane of joints.

2. ANATOMY AND AETIOLOGY

(1) True bursae

The subdeltoid bursa lies between the supraspinatus tendon covering the greater tuberosity of the humerus beneath, and the deltoid muscle and acromion process above and externally. It may be the seat of an acute gonococcal or pneumococcal bursitis, especially in young women, and of a chronic tuberculous infection, but is rarely affected either by injury or by ascending lymphatic-borne infection from the upper extremity.

The olecranon bursa lies superficially between the skin and the proximal two-thirds of the olecranon process. It is vulnerable to direct injury from which an acute bursitis may result; it is also prone to an ascending lymphatic

stream from a distal focus. Infection caused by direct implantation is likely to be staphylococcal, whereas that carried by the lymphatics is due either to staphylococci or streptococci. Although the infective process is primarily confined to the bursa, pus readily erupts through the capsule and a spreading cellulitis will result; in neglected cases the underlying bone or joint may be involved or a fungating mass be present upon the surface (Fig. 315).

In its early stages a bursa full of pus is exactly comparable to a localized abscess and should be treated as such, the patient being confined to bed. If the organism is penicillin sensitive—as it is likely to be—all pus should be removed by aspiration and 2–4 cubic centimetres of penicillin solution (500 units per cubic centimetre) injected, the limb immobilized and elevated, and systemic penicillin therapy instituted. In later stages incision and drainage will be needed.



Fig. 315.—Fungating mass resulting from delayed treatment of an acute suppurative prepatellar bursitis.

(2) Gonococcal bursitis

This lesion is an example of a haematogenous infection and Neisserian cocci seem to have a curious predilection for the subdeltoid bursa which is affected more commonly than all others. Moreover, the majority of cases are in females in the third decade of life. So true is this, that acute subdeltoid bursitis in a young woman should invariably lead to a bacteriological examination of the genital tract. It is rare for pus to form in the closed metastatic lesions of gonorrhoea and the subdeltoid bursa is no exception to this rule. Treatment consists in immobilization of the arm in abduction and an intensive course of penicillin to eradicate both the primary focus and its complications.

(3) Tuberculous bursitis

This manifestation of tuberculosis is rarely seen in true bursae, except those which communicate with a joint. As in tenosynovitis two types are seen, fluid and dry. The former is characterized by an effusion in which melon-seed bodies form, whereas the latter tends to caseate. Closed bursae should be excised immediately the diagnosis is made: those associated with joints merely share in the treatment appropriate to the arthritis.

(4) Syphilitic bursitis

A transient effusion may be seen in any bursa during the secondary stage. Later, a diffuse gummatous process may affect the ischial and prepatellar bursae, and ulceration through the overlying skin is liable to follow. The condition is frequently bilateral and this observation should always raise the

hipjoint, with which it usually communicates. This, however, is not always the case and chronic serous bursitis, often bilateral, may be seen unrelated to hip disease.

(3) Adventitious bursae

These occur in any situation in which ill-protected bony points are liable to sustained pressure. They will be described below.

3. INJURIES

(1) Penetrating wounds

Bursae may be opened by incised or punctured wounds. Clearly this type of injury will usually affect the more superficial bursae such as the olecranon and prepatellar. The former can also be opened by a fall upon the point of the olecranon when the elbow is fully flexed, the skin and bursal wall being split by tension. The injury to the bursa may be recognized by the escape of sticky synovial fluid. These simple wounds are treated according to general principles with primary suture, immobilization and chemotherapy. Occasionally, especially in the olecranon bursa, a chronic sinus persists, in which case the bursa must be completely removed.

(2) Acute traumatic bursitis (non-penetrating)

This follows a contusion after which a rapid effusion into the bursa occurs, and a circumscribed swelling rapidly makes its appearance. Again, this condition is found most frequently in superficially placed bursae. Although the overlying skin may be bruised all signs of inflammation are absent. The fluid should be removed by aspiration and the parts firmly strapped.

(3) Haemorrhagic bursitis

This is a variety of the above, the sac filling with blood. Treatment consists in aspiration and strapping.

(4) Chronic serous bursitis

The classic example is "housemaid's knee" due to repeated trauma of minor degree such as is inseparable from work which entails constant kneeling. An effusion fills the bursa and a soft fluctuating swelling results. Should the causative trauma be continued, fibrin is slowly deposited on the walls, the swelling becomes firmer, and fluctuation is less easily elicited. Finally, the cavity is almost completely obliterated and a chronic fibroid bursitis has been established. In the early stages aspiration of the fluid, firm strapping and the removal of the causative factor should lead to complete subsidence of the swelling, but this is likely to recur should the chronic irritation be resumed. Excision will then be needed.

4. INFECTIONS

(1) Acute suppurative bursitis

Purulent infections result from: (a) incised wounds, (b) punctures, (c) spread from adjacent structures, (d) spread by blood stream and (e) spread by lymph

precaution be neglected, the incision may fail to heal and a most persistent ulcer cause considerable anxiety to both patient and surgeon.

(3) Prepatellar bursa

Prepatellar bursitis gives rise to a spherical swelling in front of the ligamentum patellae, and may reach a large size. Unless inflamed, it causes no symptoms except slight tenderness on pressure. Drainage is rarely needed owing to the efficacy of aspiration and penicillin replacement. Should it be necessary, a 1½-inch incision is made at the lateral margin of the swelling, and the bursa opened from the side. Chronic enlargements require complete excision. A horseshoe incision with its convexity upwards is made (Fig. 317) and the skin flap reflected, and the bursa is dissected out with ease. The incision should not be made with its convexity downwards as this results in a scar ill-placed to withstand pressure.

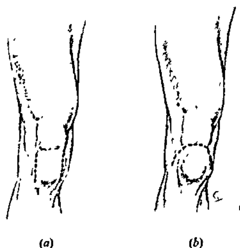


FIG. 317.—(a) Incisions for drainage of prepatellar bursa. (b) Incision for complete excision.

An alternative method of treatment is to empty the bursa by aspiration and to inject a sclerosing fluid such as sodium morrhuate. The results are not altogether satisfactory, but if excision is contra-indicated this procedure should be given a trial.


FIG. 318.—Massive adventitious bursa over the acromion process; the so-called "deal-runner's shoulder".

(4) Semimembranosus bursa

Semimembranosus bursitis is characterized by the presence of a spherical swelling in the popliteal space, more readily felt when the knee is flexed. It causes mild, aching pain and a feeling of slight insecurity of the joint. The bursa is approached either through a vertical incision along the semimembranosus tendon or by a transverse cut on the postero-internal aspect of the popliteal fossa. Other bursae so rarely call for surgical treatment that no formal methods of approach need description.

6. ADVENTITIOUS BURSAE

These are of new formation over bony prominences subjected to constant pressure, for example:

suspicion of syphilis, and a complement fixation test should be applied. Treatment follows the usual anti-syphilitic routine.

(5) Gouty bursitis

This results from the deposition of sodium biurate in the walls of a bursa, most commonly the olecranon. Large swellings form, and the skin gives way, leading to a gouty ulcer. Treatment is by excision.

5. CLINICAL SIGNS AND SURGICAL TREATMENT OF INDIVIDUAL BURSAE

(1) Subdeltoid bursa

Subdeltoid bursitis leads to a ballooning outwards of the deltoid curve of the shoulder region. Should the swelling be of a considerable size it will bulge either in front of or behind the margin of the muscle, more probably the former. It causes pain, tenderness and limitation of movement, the patient finding most relief when the shoulder is supported in abduction to 90 degrees. The joints should therefore be immobilized in this position and midway between internal and external rotation, whilst appropriate treatment is directed to the cause. Drainage is rarely needed, but should this be required, an incision is made along the anterior margin of the deltoid muscle over the area of maximal swelling. Rarely, a chronic fibroid condition associated with the deposition of calcareous plaques is seen in this bursa and in that case a radical excision will be required. Access will be obtained through a long incision at the anterior margin of the deltoid.

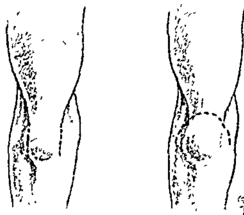


FIG. 316.—(a) Incisions for drainage of olecranon bursa placed well away from the midline. (b) Incision for complete excision.

(2) Olecranon bursa

Olecranon bursitis presents as a superficial swelling over the bony process. Pain is present only in an acute inflammatory lesion. Drainage of this bursa should always be avoided if possible, and aspiration with penicillin replacement given a prolonged trial. In chronic enlargements the bursa should be removed intact. A horseshoe incision is made with its convexity upwards and the flap of skin reflected downwards, the sac thus being exposed (Fig. 316). Its dissection is often unexpectedly difficult, as the thin walls tend to be adherent both to the skin and periosteum. Nevertheless, it is essential that no particle of lining membrane be left, lest a persistent sinus results. In few other situations does so simple an incision demand so complete immobilization until the wound is soundly healed. Should this

NOTE.—Upon completion of the whole work an exhaustive analytical Index will be published in a separate volume. Each individual title in this volume has been separately indexed, and its subject-matter subdivided beneath that main title; additional references and cross-references beyond this, under the name of any particular subject, have been included. No attempt has been made to include references to subject-matter appearing in this volume which is dealt with fully in other volumes, although in one or two instances it has been possible to give the volume in which this subject is appearing.

THE PUBLISHERS

INDEX TO VOLUME 2

A

(1) the "deal-runner's shoulder" (Fig. 318).
(2) the "Covent Garden hummy" over the seventh cervical vertebra.
(3) the "basket-carrier's bursa" in the scalp.
(4) the "tailor's ankle", a bursa over the external malleolus.
(5) those over exostoses, hallux valgus and deformed feet.

Should these be causing inconvenience they should be excised.

Figs. 313, 314, 315 *and* 318 *are reproduced by courtesy of E. and S. Livingstone, Ltd.*

[References to other titles are given under Bursae in the Index Volume.]

CAECOSTOMY

See Colitis

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